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N-胺基吡啶盐作为氮自由基前体在可见光诱导碳氮键形成反应中的进展

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摘要 由于吡啶盐的氧化还原性质，人们发现稳定的吡啶盐在自由基化学中起着重要作用. 吡啶盐容易经历单电子还原和N—N键断裂以传递N自由基. 综述了近三年来*N*-胺基吡啶盐作为氮自由基前驱体在可见光诱导碳氮键形成反应中的研究进展. 根据反应底物的不同，综述分为三个部分：与芳烃的反应、与烯烃的反应及与烷烃的反应.
关键词 吡啶盐；自由基；可见光；绿色有机合成

Progress of *N*-Amino Pyridinium Salts as Nitrogen Radical Precursors in Visible Light Induced C—N Bond Formation Reactions

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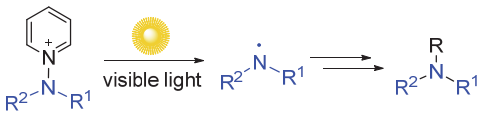
Abstract Because of the redox properties of pyridine salt, it is found that *N*-amino pyridine salt plays an important role in free radical chemistry. *N*-Amino pyridinium salts easily undergo single electron reduction and N—N bond fragmentation to deliver N radicals. In this review, the advances of *N*-amino pyridinium salt serves as a powerful nitrogen radical precursor in visible light induced reactions for C—N bond formation are summarized in the last three years. According to the reaction substrates, the review is divided into three parts: react with arenes, react with olefins, and react with alkanes.
Keywords pyridinium salts; radical; visible light; green organic synthesis

Free radical reaction plays an important role in organic chemical transformation.[1] In recent years, nitrogen radical mediated organic chemical reactions have received more and more attentions.[2] There are several ways to generate nitrogen free radicals, among which the reaction of generating nitrogen free radicals from pyridinium salts has achieved much progress. In general, the bench-stable and readily available pyridinium salts that are highly reactive species that can undergo various reactions, such as nucleophilic addition and 1,3-dipolar addition. However, pyridinium salts have not been used in free radical reactions until recent years. Pyridinium salts easily undergo single electron reduction and N—N bond fragmentation to deliver N radicals. Because of the redox properties of pyridine salt, it is found that stable pyridine salt plays an important role in free radical chemistry (Scheme 1). At present, alkyl radicals, trifluoromethyl radical, N-centered radicals, *O*-centered radicals as well as other related radicals could all be well generated from corresponding pyridinium salts, which provide a powerful approach for the construction of C—C and C—X bonds.[3] In this review, the advances of pyridinium salts serves as a powerful nitrogen radical precursors in visible light induced reactions for C—N bond



Scheme 1 *N*-Amino pyridinium salts as nitrogen radical precursors

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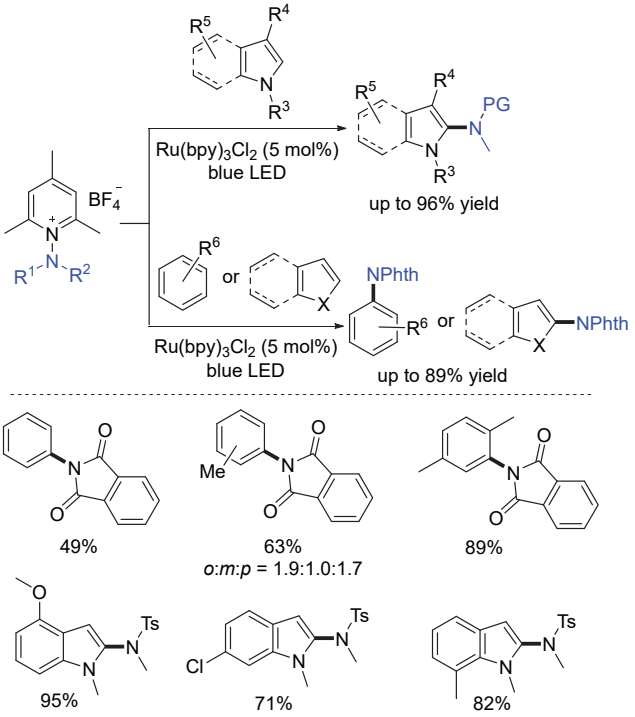
formation was summarized in the last three years.

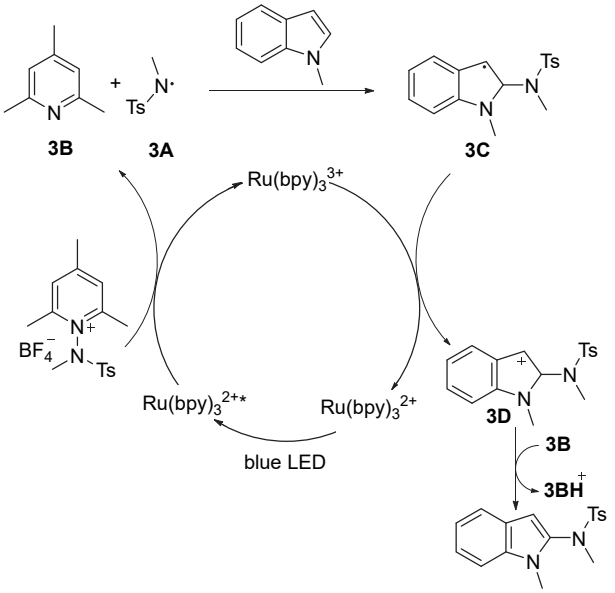
1 React with arenes

In 2015, Studer *et al.*[4] found that pyridinium salts were efficient N-radical precursors which are easily accessible from cheap starting materials. The pyridinium salts can be used for regioselective radical amidation of heteroarenes and substituted arenes using $Ru(bpy)_3Cl_2$ as the photocatalyst (Scheme 2). Single electron reduction of pyridinium salts was proposed for the generation of nitrogen radicals. The reagent design allows for simple changes in the substituents on the amidyl radical. Therefore, the reactivity of the pyridinium salts can be easily adjusted to the free radical receptor. The results of cyclovoltammetry for pyridinium salts showed irreversible reduction at −0.75 and −0.70 V vs Ag/Ag^+, respectively.



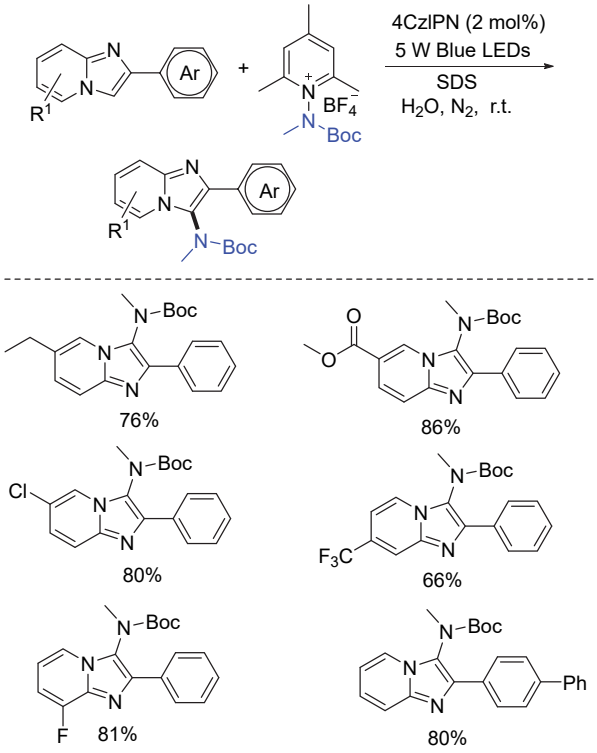
Scheme 2 Amidation of arenes and heteroarenes

The suggested mechanism is described in Scheme 3.[4] In the first step, irradiation of $Ru(bpy)_3^{2+}$ by blue light gives the excited $Ru(bpy)_3^{2+*}$. This excited species reduces pyridinium salt by single-electron transfer (SET). Fragmentation of the pyridinium salts with $Ru(bpy)_3^{2+*}$ leads to the sulfonamidyl radical **3A** and pyridine **3B**. The regioselectively reaction of amidyl radical **3A** with *N*-methylindole affords radical **3C**. Then radical **3C** is oxidized by $Ru(bpy)_3^{3+}$ to give $Ru(bpy)_3^{2+}$, along with the release of the cationic species **3D**. Finally, the desired product was generated via deprotonation of **3D**, with the assistance of pyridine **3B** which formed in the fragmentation acts as a base.



Scheme 3 Suggested mechanism

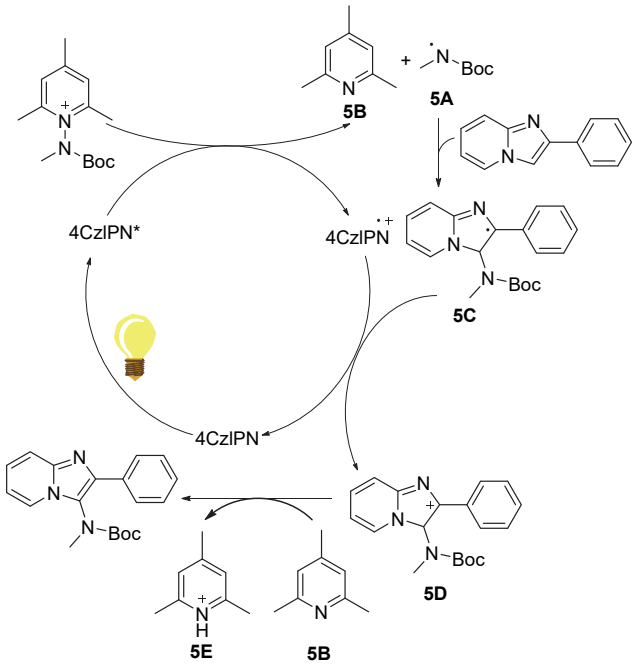
A light-promoted metal-free amination of imidazo[1,2-*a*]pyridines with *N*-aminopyridinium salt by the assistance of surfactants in water was reported by Li group[5] (Scheme 4). The micelles formed by the amphiphilic anionic surfactant sodium dodecyl sulfate (SDS) not only increase the concentration of polar cation *n*-aminopyridine salt on the negatively charged surface of the micelles, but also in-



Scheme 4 Visible-light mediated imidazo[1,2-*a*]pyridine C—H amination with *N*-aminopyridinium salt accelerated by surfactant in water

crease the concentration of lipid-soluble imidazolidine [1,2-*a*]pyridine and photocatalyst in the hydrophobic core of the micelles, which effectively solves the mass transfer problem in water and greatly facilitates the reaction. The electrostatic interaction between positively charged *N*-aminopyridinium and negatively charged surface of micelles is of great significance in this method.

The proposed reaction mechanism is described in Scheme 5.[5] Firstly, 4CzIPN is excited by blue light to form 4CzIPN*. With the assistance of micelle effect, N-radical could be generated easily from the reaction of *N*-aminopyridinium salt with 4CzlPN* under the visible-light irradiation in water. Then, radical **5C** is afforded from the reaction of N-radical **5A** with imidazo[1,2-*a*]pyridine. After SET oxidation of **5C**, cationic species **5D** is given. Finally, desired product is isolated by deprotonating of cationic species **5D** in the presence of pyridine.

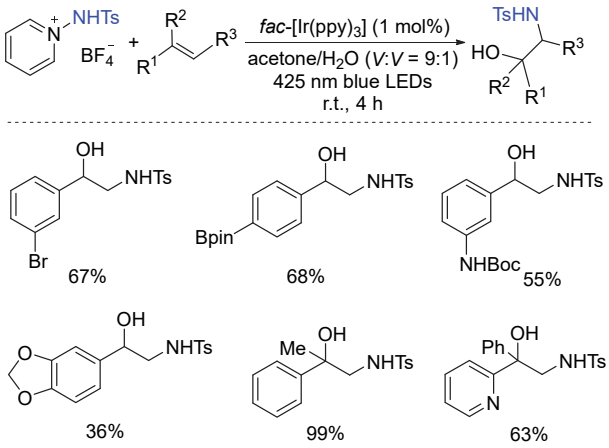


Scheme 5 Proposed reaction mechanism

2 React with alkenes

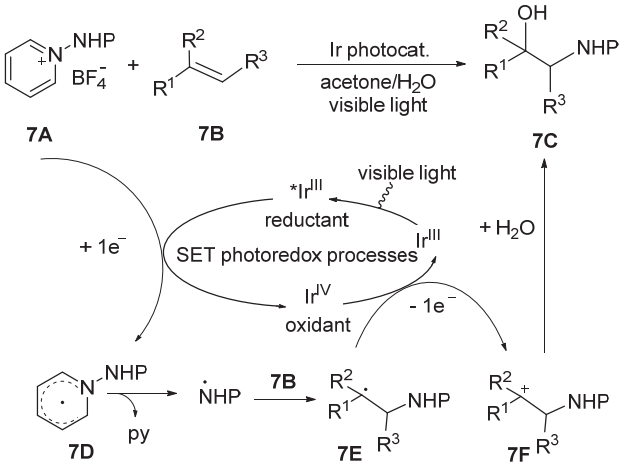
In 2015, the aminohydroxylation of olefins using pyridinium salts in the present of photoredox catalysis was developed by Akita group[6] (Scheme 6). The present aminohydroxylation is regiospecific reaction for both terminal and internal alkenes regardless of acyclic and cyclic structure. Series of vicinal amino alcohol derivatives with various functional groups can be obtained under mild reaction conditions with easy handling. Well-designed N-protected 1-aminopyridinium salts serve both as an electron acceptor and as an efficient amidyl radical precursor in this system.

Whether *E*- or *Z*-*β*-methylstyrene was subjected to this aminohydroxylation reaction, the corresponding products with very similar diastereoselectivities were isolated



Scheme 6 Scope of the photocatalytic aminohydroxylation

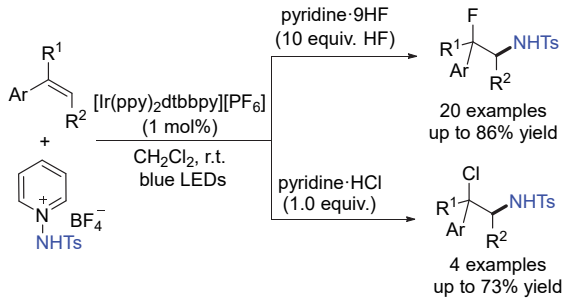
(Scheme 7), indicating that the present photocatalytic aminohydroxylations proceed via the same intermediate irrespective of the starting *E*- and *Z*-alkenes. Control experiments were conducted. The results strongly support that radical intermediates are involved in the present reaction. On the basis of these results, a plausible reaction mechanism is proposed as shown in Scheme 7.[6] Firstly, the excited species $*Ir^{III}$ is obtained via the irradiation of photocatalyst Ir^{III} by visible light, which undergoes SET reaction with amino pyridinium **7A** to afford stabilized radical **7D** and highly oxidizable species Ir^{IV}. Then the amidyl radical reacts with alkene **7B** in regiospecific manner to yield radical intermediate **7E**, which is oxidized by the strongly oxidizing species Ir^{IV} to afford *β*-amino-carbocationic intermediate **7F** with the regeneration of the ground state photocatalyst Ir^{III}. Finally, the desired product 1,2-aminoalcohol is generated from the nucleophilic reaction of the carbocationic intermediate with H_2O.



Scheme 7 Proposed reaction mechanism

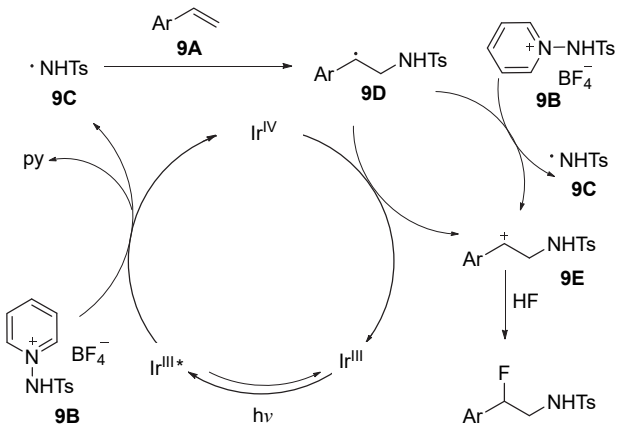
In 2018, the high regioselective aminofluorination of styrenes mediated by visible light was developed by Xu group[7] (Scheme 8). In the presence of shelf stable *N*-Ts-protected 1-aminopyridine salt as the nitrogen-radical precursor, and the commercially available hydrogen fluoride-

pyridine as the nucleophilic fluoride source, the products can be generated in moderate to high yields. Unfortunately, the reaction did not afford the desired product when trisubstituted unsymmetric alkenes such as but-2-en-2-yl benzene was used as a substrate. Additionally, aminochlorination of alkenes using pyridine hydrochloride as the Cl donor also realized. *β*-Bromoamines could also be isolated using pyridine hydrobromide as the bromide donor, albeit with a low yield of 17%.



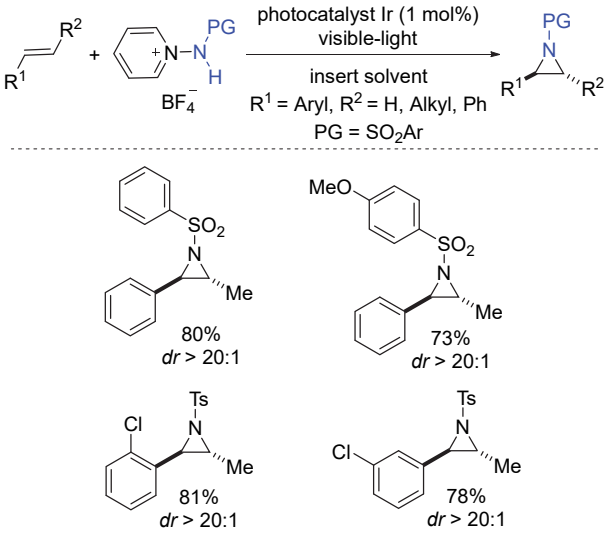
Scheme 8 Regiospecific three-component aminofluorination of olefins via photoredox catalysis

2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) trapping experiments were carried out, showing that radical process was possible for this aminofluorination process. The putative mechanism is illustrated in Scheme 9.[7] First, the photocatalyst $Ir(ppy)_2(dtbbpy)PF_6$ (Ir^{III}) is excited by visible light to afford the excited species (Ir^{III}*). Then oxidative quenching of excited species (Ir^{III}*) with *N*-Ts-protected aminopyridine salt **9B** occurs to give the corresponding radical **9C**, with the liberation of highly oxidizable species Ir^{IV}. Subsequently, a regiospecific addition reaction of N-centered radicals with the alkene gives stabilized radical intermediate **9D**, which is converted to cationic intermediate **9E** via oxidation by species Ir^{IV}. Finally, the cationic intermediate **9E** is trapped by hydrogen fluoride-pyridine to provide the final product. Alternatively, a chain mechanism is also possible: benzyl radical intermediate **9D** is oxidized by the *N*-Ts-protected 1-aminopyridine salt to provide the cationic intermediate **9E**.



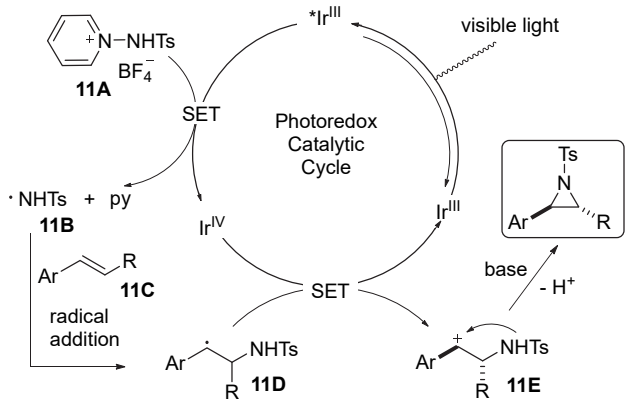
Scheme 9 A proposed mechanism

Xu group[8] developed a novel method for the synthesis of substituted aziridines from the reaction of alkenes and N-protected 1-aminopyridinium salts induced by visible light (Scheme 10). It is interesting to note that the identical *trans*-diastereoisomer was formed, whether *E*- or *Z*-stilbenes were subjected to this reaction. Additionally, one-pot, three-component reaction involving iminothiazolidine, *α*-amino ketone or N-PFB-protected respectively is successfully realized, showing the generality and synthetic value of this catalytic protocol.



Scheme 10 Alkene functionalization for the stereospecific synthesis of substituted aziridines by visible-light photoredox catalysis

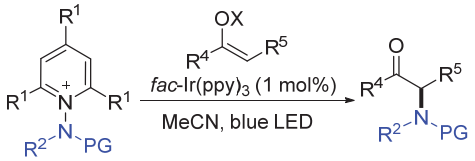
Control experiments were conducted to gain some insight into the mechanism. The possible reaction mechanism is illustrated in Scheme 11.[8] The photocatalyst $Ir(ppy)_2(dtbbpy)PF_6$ (Ir^{III}) undergoes a metal-to-ligand charge-transfer (MLCT) process under visible-light irradiation to form the excited state ($*Ir^{III}$). Then oxidative quenching of the excited state ($*Ir^{III}$) by *N*-Ts-protected 1-aminopyridium **11A** occurs to generate the nitrogen-centered radical species, which simultaneously generates $Ir(ppy)_2(dtbbpy)^+$ (Ir^{IV}). The addition reaction of electrophilic radical with the alkene delivered intermediate **11D** gives car-



Scheme 11 Proposed mechanism

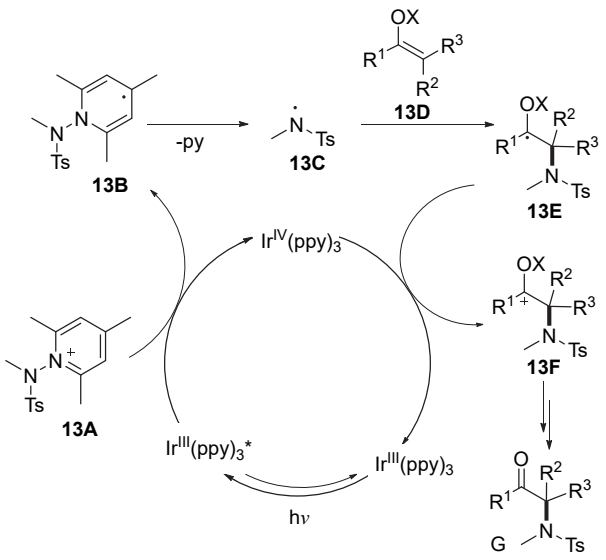
bocation intermediate **11E** via oxidization by Ir^{IV}, along with the formation of photocatalyst Ir^{III}. Finally, a carbocation intermediate is captured by the nucleophilic nitrogen of the sulfonamide, providing the final product via deprotonation.

Gryko group[9] found that the visible-light-mediated amination of π-nucleophiles with *N*-aminopyridinium salts is also possible (Scheme 12). Nitrogen-centered radicals can be trapped by enol equivalents to give *α*-amino carbonyl compounds in excellent yields. The substitution pattern of the salts has an effect on the reactivity of the generated electrophilic N-centered radicals. Boc, trifluoroacetyl, or pentafluorobenzoyl substituents enable effective enol functionalization, while *N*-Cbz protected salts are less reactive. Ketones, aldehydes, esters enol equivalents, vinyl ethers, and 1,3-diketones are all suitable for this reaction, showing broad synthetic utility of this method. For structurally similar mono-protected salts, a compound which has a higher reduction potential could provide the product with a higher reaction yield.



Scheme 12 Amination of π-nucleophiles

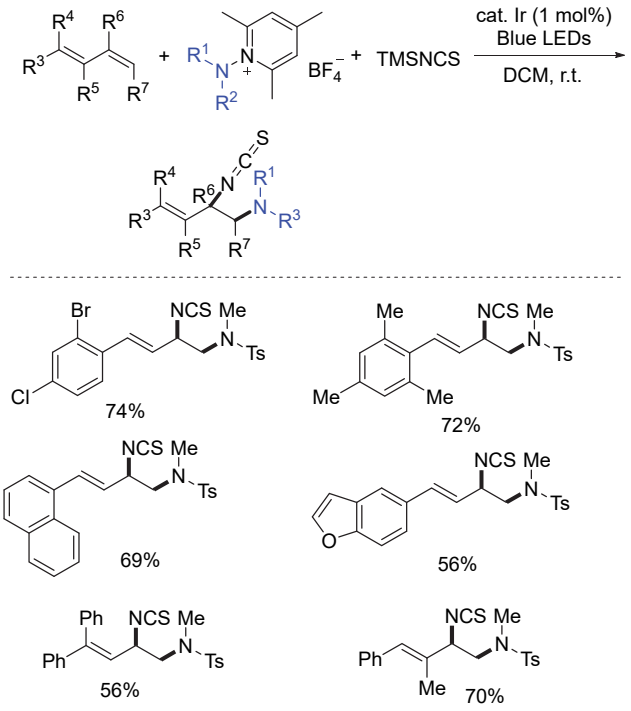
Experiments such as high resolution mass spectra (HRMS) analysis, Stern-Volmer experiments and electron paramagnetic resonance (EPR) measurements were conducted to investigate the mechanism of this reaction (Scheme 13). The results imply that efficient radical chain processes are unlikely. The possible reaction mechanism is depicted in Scheme 13.[9] The reduction of Ir-catalyst with *N*-aminopyridinium salt occurred via single electron transfer to provide pyridyl radical **13B** and Ir(IV), then



Scheme 13 Plausible mechanism of the amination of π-nucleophiles

pyridyl radical undergoes fragmentation to give N-centered radical and a rearomatized pyridine derivative. N-Radical can be trapped by π-nucleophile **13D** to produce radical **13E**, which was oxidized to cation **13F** by Ir(IV), along with the formation of the Ir(III) catalyst. Subsequently, the desired products are generated via deprotection of the acyl or silyl group from cation **13F**.

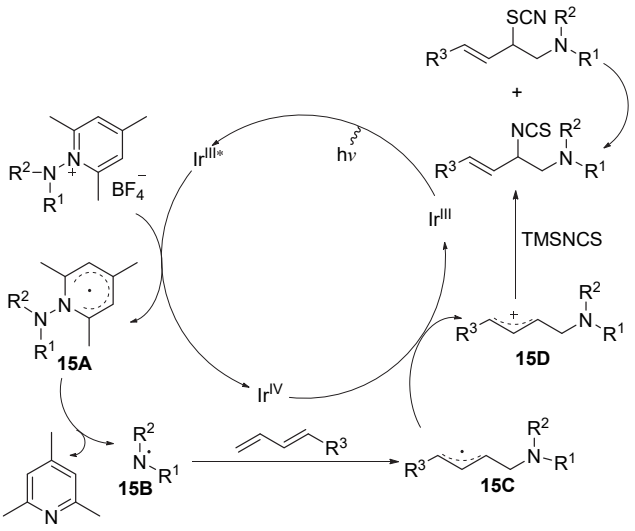
Selective functionalization of 1,3-diene is an extremely challenging but valuable synthetic transformation, because it can convert readily available chemicals into highly functional molecules. In 2021, Zhu group[10] reported the reaction of conjugated dienes with *N*-aminopyridinium salts and trimethylsilylisothiocyanate (TMSNCS), affording 1,2-aminoisothiocyanation in a highly chemo- and regioselective manner under mild photoredox catalytic conditions (Scheme 14). It should be noted that when a mixture of *E*/*Z* diene mixture is used as starting material, only *E*-olefins are separated. Mechanistic studies indicate that the facile isomerization of allyl thiocyanates to allyl isothiocyanates under photocatalytic conditions is responsible for the selective formation of the observed products. Control experiments showed that photooxidation catalyst and blue LED irradiation were essential for this isomerization. The light on/off experiments showed that the product was formed only under blue LEDs irradiation.



Scheme 14 Selective 1,2-aminoisothiocyanation of 1,3-dienes

The plausible reaction pathway is illustrated in Scheme 13.[10] Reduction of *N*-aminopyridinium salt by excited Ir^{III*} affords radical **15A** and Ir^{IV} (Scheme 15). Then N—N bond cleavage of radical **15A** occurs to afford the nitrogen-centered radical **15B** and 2,4,6-collidine. Allylic radical **15C** is produced by regioselective addition of radical

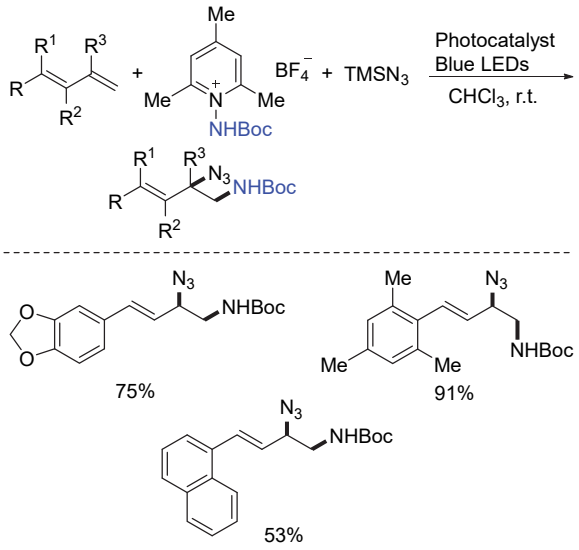
15B to the 1,3-diene. Subsequently, radical **15C** is oxidized by Ir^{IV} to afford carbocation intermediate **15D**, with concurrent liberation of Ir^{III} species. TMSNCS is highly regionally selective, albeit chemically less selective, for the off-catalytic cycle nucleophilic addition of allyl cation **15D** to provide a mixture of 1,2-amino-isothiocyanates and 1,2-amino-thiocyanates products. However, the latter is cleanly converted *in situ* into the former with extended reaction time.



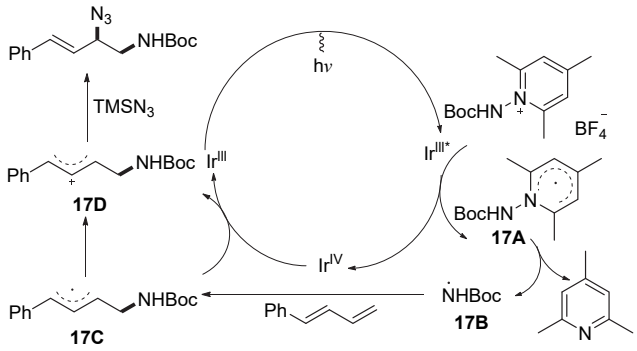
Scheme 15 Proposed catalytic cycle

Although functional allyl azides have obvious synthetic potential, only limited synthetic routes have been developed. Zhu group[11] described a three-component 1,2-amidoazidation of 1,3-dienes reaction of 1-aryl substituted 1,3-dienes with *N*-amidopyridinium salt and trimethylsilyl azide ($TMSN_3$), affording exclusively the 1,2-amidoazidation products smoothly in the presence of *fac*-Ir(ppy)$_3$ under blue LED irradiation (Scheme 16). Additionally, the 1-alkyl substituted counterparts undergo the same reaction with moderate to high 1,2- vs 1,4-selectivity. It is interesting to note that amidoazidation of styrenes under standard conditions also occurs smoothly to afford products in moderate yields.

Control experiments were conducted and indicated that both the photoredoxmcatalyst and the blue LED irradiation are important for this three-component reaction.[11] On the basis of these control experiments, a plausible reaction pathway is described in Scheme 17. Radical **17A** is formed via reduction of *N*-amidopyridinium salt by excited Ir^{III}* species, which followed by fragmentation to afford nitrogen radical **17B** and 2,4,6-collidine. Regioselective addition of nitrogencentered radical **17B** to 1,3-diene occurs to give allylic radical **17C**, then oxidation of allylic radical **17C** by Ir^{IV} provides the allylic cation **17D**, with simultaneously liberation of the ground state Ir^{III} catalyst. Finally, the corresponding product is generated from regioselective nucleophilic addition of azide to allylic cation **17D**.



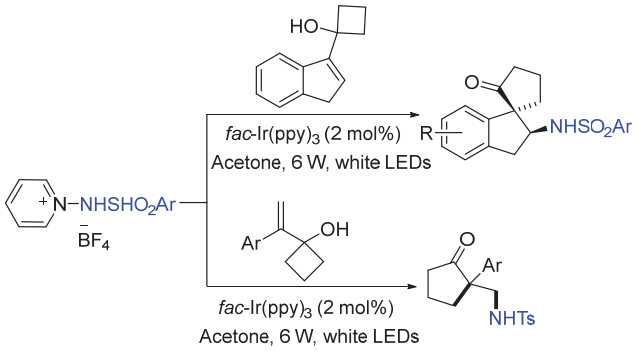
Scheme 16 Photoredox catalytic three-component amidoazidation of 1,3-dienes



Scheme 17 Proposed reaction mechanism

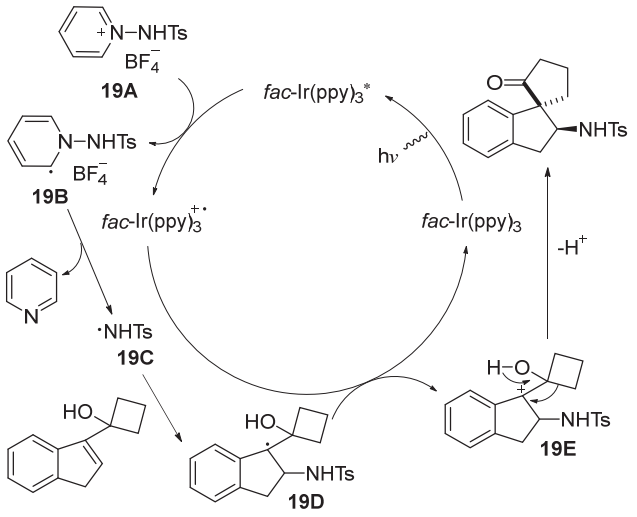
β-Aminoketones and their derivatives not only have a variety of biological activities, but also are important synthetic cornerstones for the preparation of many drugs and natural products. The visible light photoredox-catalyzed N-centered radical addition/semipinacol rearrangement cascade of cycloalkanol-substituted 1*H*-indenes or styrenes with *N*-arylsulfonyl protected 1-aminopyridinium salts is described by Xiao group[12] (Scheme 18). Various of *β*-amino (spiro)cyclic ketones can be obtained using this strategy from easily available starting materials. A gram-scale reaction was performed to showing the synthetic utility of the photoredoxmediated N-centered radical addition/semipinacol rearrangement cascade reaction.

A radical trapping experiment implies that a radical process is involved in the cascade reaction. A plausible mechanism for the N-centered radical addition/semipinacol rearrangement cascade is shown in Scheme 19.[12] Initially, the SET reduction of **A** by photoexcited *fac*-Ir(ppy)$_3$* induced by visible light occurs to provide the radical **19A** and oxidizing state *fac*-Ir(ppy)$_3^{+\bullet}$. Subsequently, the N-centered radical **19C** is generated from a homolytic N—N single bond cleavage, along with the release of a pyri-



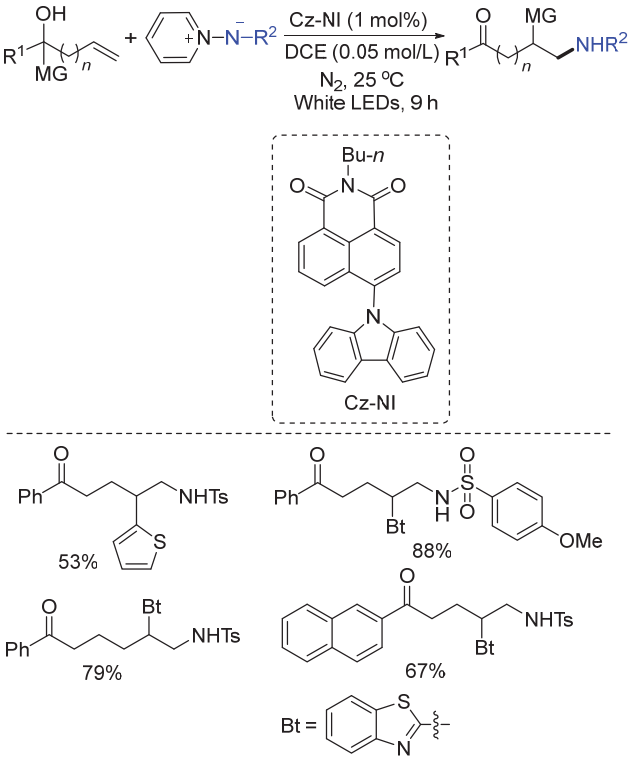
Scheme 18 N-Centered radical addition/semipinacol rearrangement for the convenient synthesis of *β*-amino (spiro)cyclic ketones

dine. The addition of N-centered radical with substrate cycloalkanol generates the more stable alkyl radical **19D**. Intermediate **19D** is converted to carbocation **19E** via oxidation by the oxidizing state *fac*-Ir(ppy)$_3^{+\bullet}$ species, which simultaneously regenerates the ground-state *fac*-Ir(ppy)$_3$. The final product is formed via the semipinacol rearrangement of the **19E** species.



Scheme 19 Proposed reaction mechanism

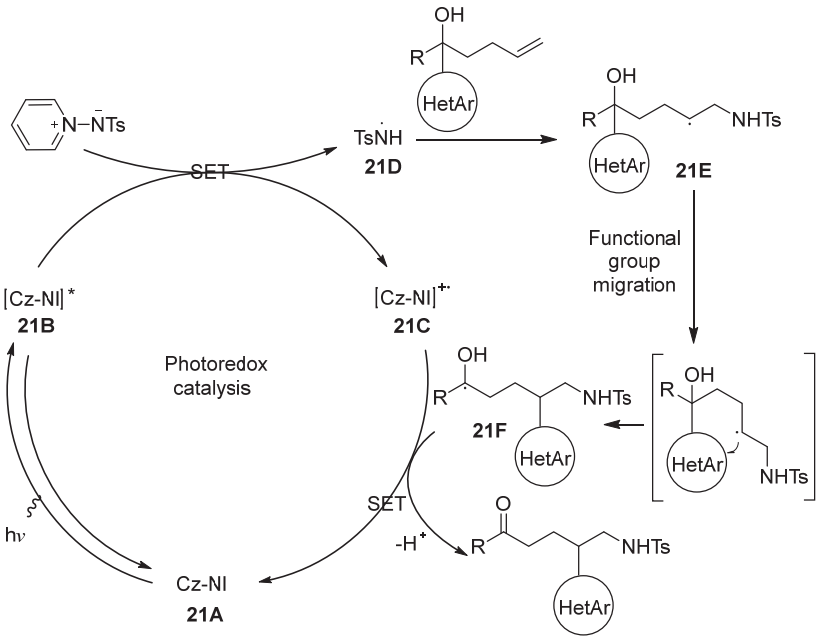
Aminoketones are an important class of compounds, which are widespread in bioactive natural products and marketed pharmaceuticals. A metal-free amino-heteroarylation of unactivated olefins for the rapid synthesis of various amino ketones under mild conditions via organic photoredox catalysis was demonstrated by Xu group[13] (Scheme 20). However, it should be noted that the migration of these functional groups requires catalytic quantities of acids as catalysis, which is mainly due to the easy formation of cyclic transition states. However, both benzoyl and Boc protected 1-aminopyridine could not provide products according to this strategy, which may be due to the less electron-withdrawing ability of these protective groups.



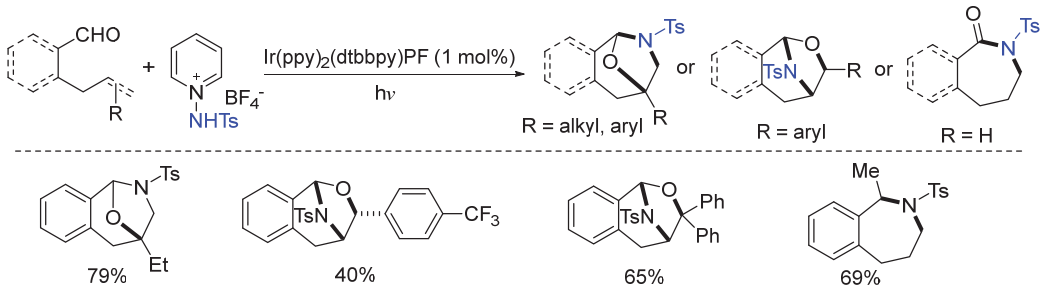
Scheme 20 Amino-heteroarylation of unactivated olefins to access distal amino ketones

A series of mechanistic experiments and density functional theory (DFT) calculations indicate that a photoredox catalytic sequential radical addition/functional group migration process is possible for this transformation.[13] An organic photoredox catalytic functional group migration process is described in Scheme 21. Firstly, the excited photocatalyst [Cz-NI]* is generated by the irradiation of white light. and then the SET reaction of substrate aminopyridinium and the [Cz-NI]* occurs to provide the critical N-centered radical species **21D**. Then N-centered radical species was added with the alkene substrate (heteroaryl-substituted tertiary bishomoallylic alcohol) to form the alkyl radical species **21E**. Subsequently, the radical species F is formed via migration of the heteroaryl group through a cyclic transition state. Finally, the single-electron oxidation, and deprotonation occur in sequence to deliver the desired product, along with the regeneration of photocatalyst [Cz-NI].

Seven-member nitrogen-containing heterocyclic framework plays an important role in natural products and pharmaceutical science. A photocatalytic tandem cyclization of *o*-alkenylbenzaldehydes using pyridinium salts as the amination reagent was realized by Xu group[14] (Scheme 22). A variety of valuable seven membered nitrogen-containing heterocyclic frameworks were prepared by a simple one-step method in moderate to excellent yields. This transformation has mild reaction conditions and good functional group tolerance. In addition, the selectivity of the reaction was explained by the combination of control experiments and DFT calculations.



Scheme 21 Proposed mechanism

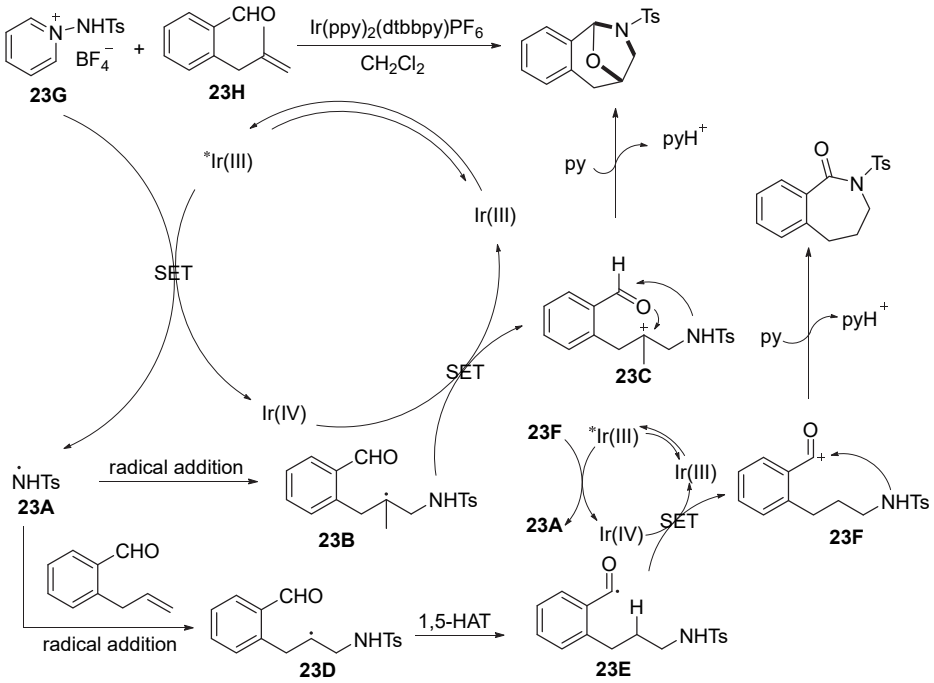


Scheme 22 1,3-Aminopyridylation of [1.1.1]propellane with *N*-aminopyridinium salts

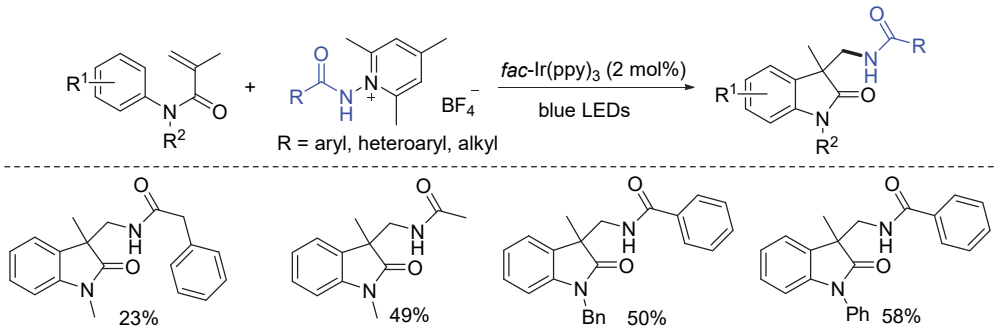
A plausible reaction mechanism is illustrated in Scheme 23.[14] Irradiation of the ground-state photocatalyst Ir(ppy)$_2$(dtbbpy)PF$_6$ with visible light affords the excited-state *Ir(III) species via a metal-to-ligand charge-transfer (MLCT) process. The excited-state *Ir(III) is oxidized to Ir(IV) species by N-aminopyridinium, along with the liberation of the nitrogen-centered radical **23A**. The electrophilic N-radical is trapped by the alkene **23H** to form a stable 3°-carbon centered radical intermediate **23B**. The stabilized 3° carbocation intermediate **23C** is formed from radical intermediate **23B** via oxidation by Ir(IV) species. Finally, deprotonation of the carbocation intermediate gives the desired product. As for substrate 1°,2°-carbon centered radical intermediate **23D** is obtained from addition of the N-radical to the olefin coupling partner. Then translocation of a proximal aldehyde hydrogen atom via 1,5-*H* atom transfer occurs to generate radical **23E**, which is oxidized by Ir(IV) to give formyl carbocation **23F**. Finally, the corresponding product is isolated through intramolecular nucleophilic attack and deprotonation.

In 2022, a visible-light-promoted intermolecular radical amidation/cyclization of arylacrylamides using *N*-aminopyridinium salts as the source of amidyl radicals was realized by Yu group[15] (Scheme 24). The reaction has the characteristics of wide range of substrates and good tolerance of functional groups. A variety of amide-tethered-oxindoles compounds were synthesized with moderate to good yields. However, *N*-disubstituted aminopyridinium salt is not effective in this system, it maybe due to the steric hindrance caused by the *N*-methyl group.

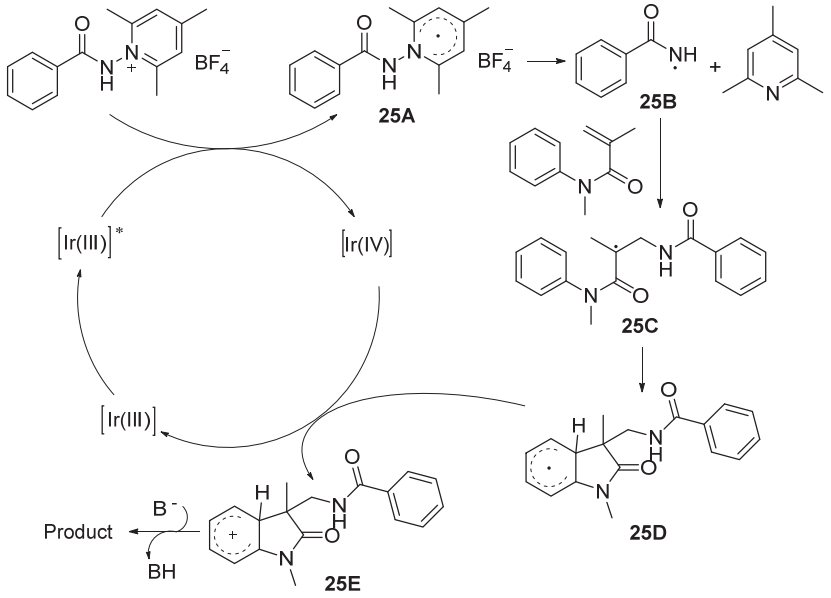
The inhibition experiment with 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) implies that radical mechanism is possible for this reaction.[15] The present transformation is believed to take place via the radical pathway shown in Scheme 25. The single electron transfer between the *N*-aminopyridinium salt and the excited [Ir(III)]* occurs to generate radical **25A** and [Ir(IV)]. The amidyl radical **25B** was formed via fragmentation of radical **25A**, which is subsequently captured by *N*-methyl-*N*-phenylmethacrylamide to produce the radical intermediate **25C**. The radical intermediate **25C** undergoes cyclization to afford radical **25D**. Radical **25D**



Scheme 23 Proposed reaction mechanism



Scheme 24 Amidation/cyclization of arylacrylamides using *N*-aminopyridinium salts



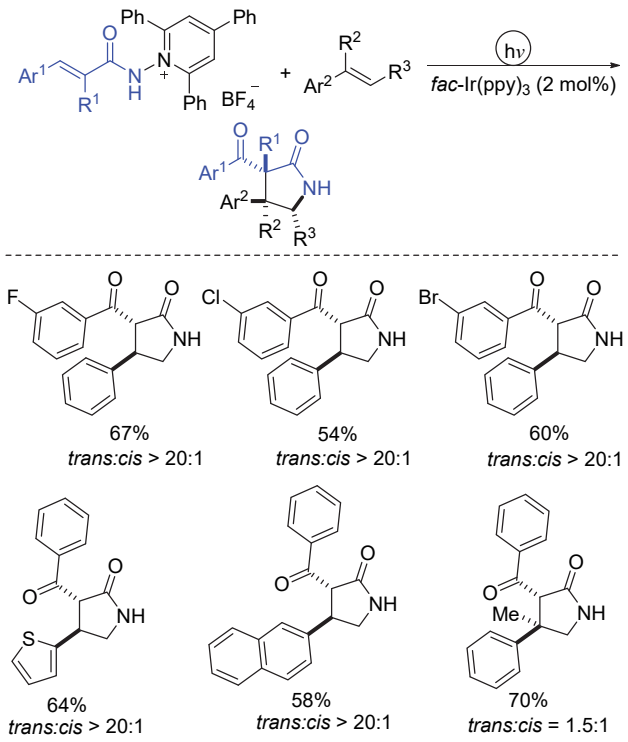
Scheme 25 Proposed mechanism of amidation/cyclization of arylacrylamides

is converted to the carbocation **25E** via oxidation by [Ir(IV)]. Finally, product is generated by deprotonation. K_3PO_4 has a favorable effect on the reaction, probably because it can improve the basicity of the system and make deprotonation easier.

The synthesis of functionalized *γ*-lactams via photoinitiated deaminative [3+2] annulation reaction of *N*-aminopyridinium salts with alkenes is realized by Xia group[16] (Scheme 26). The key amidyl radical intermediates generated from the employed *N*-aminopyridinium salts through N—N bond cleavage via a photoinduced SET process was proposed for this transformation. This synthetic method afforded a broad substrate scope and excellent control of the diastereoselectivity for most of the *γ*-lactam products, significantly improving the diversity of *γ*-lactam synthesis.

A plausible reaction mechanism is illustrated in Scheme 27.[16] The irradiation of the photocatalyst (PC) by visible light generates its excited state (PC*). Then, oxidation of photocatalyst with Katritzky salt via SET leads to its radical cation ($PC^{+\bullet}$), with the formation of an amidyl radical **27A** through the N—N bond cleavage. Subsequent a stabilized benzylic radical intermediate **27B** which is generated form intermolecular radical addition of the resulting N-centered radical **27A** to the double bond of styrene undergoes intramolecular 5-*exo*-*trig* cyclization to give key intermediate **27C**. Then intermediate **27D** is generated from intermediate **27C** via oxidation reaction with the PC radical cation ($PC^{+\bullet}$), which follows by the nucleophilic addition of dimethyl sulfoxide (DMSO) to provide the final product.

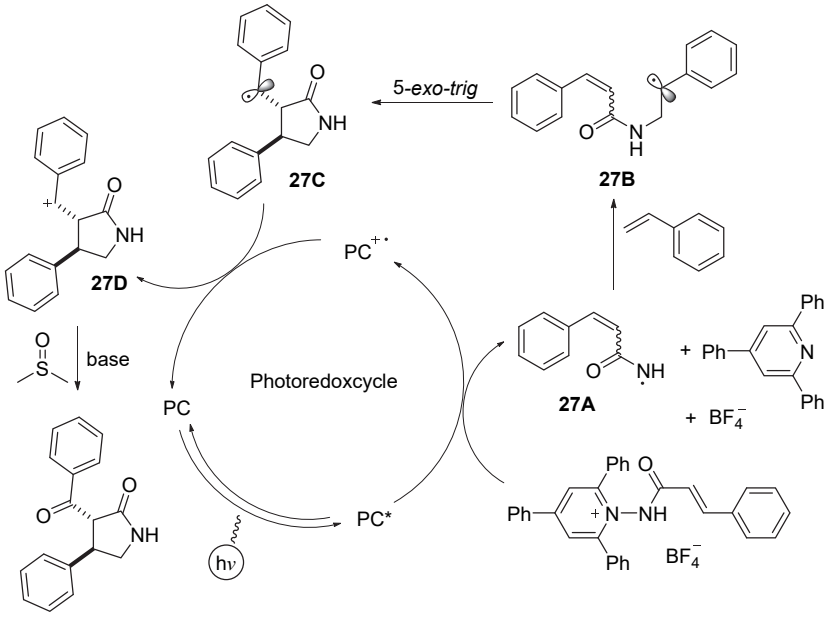
The visible light induced annulation reactions of *N*-aminopyridinium salts with alkenes using *fac*-Ir(ppy)$_3$ as catalyst were realized by Yu group.[17] This reaction can yield two different types of products: in the case of vinyl arenes, the [3+2] cyclization product dihydrooxazole



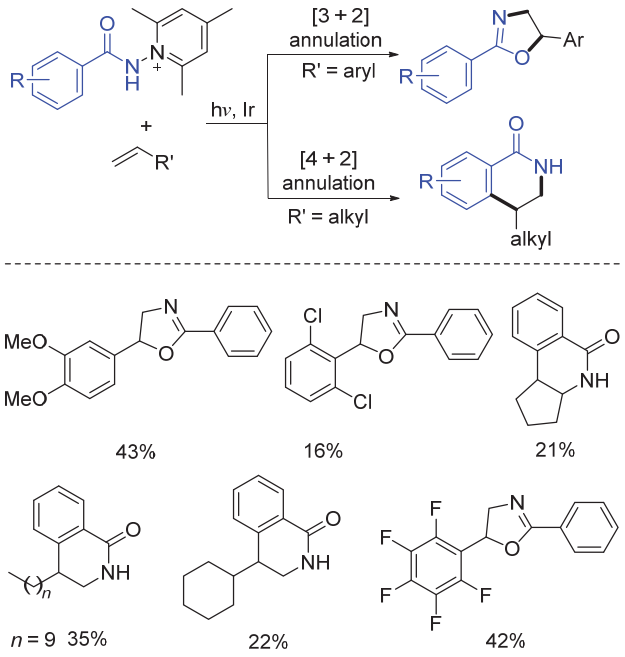
Scheme 26 Synthesis of *γ*-lactams enabled by photoinduced deaminative [3+2] annulation reaction

yields only; on the other hand, when alkyl-substituted alkenes are used, it provides [4+2] cyclization product dihydroisoquinolinone. The influence of the alkenes on the reaction consequence is rationalized by theoretical calculations.

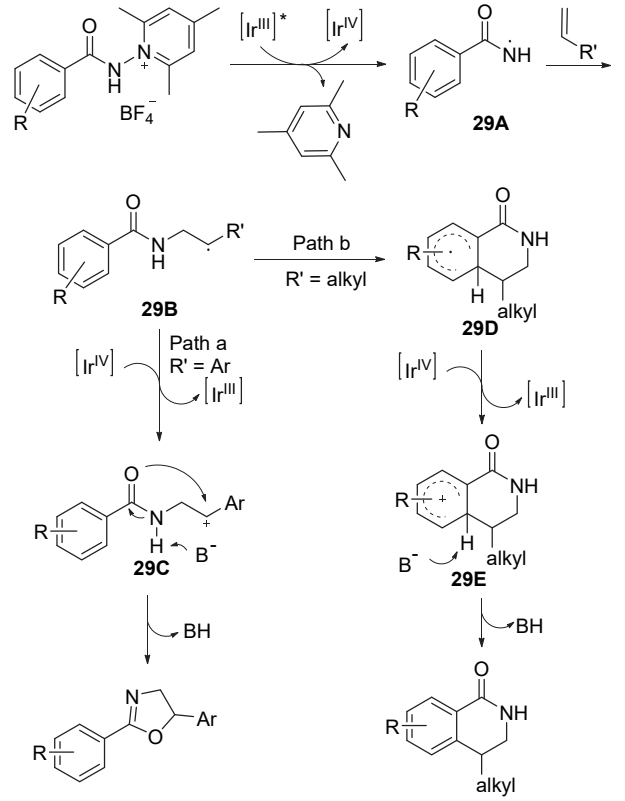
The formation of dihydrooxazole and dihydroisoquinolinone is described by the mechanisms which is depicted in Scheme 29. Firstly, single electron reduction of *N*-aminopyridinium salts by photoexcited *fac*-Ir(ppy)$_3^*$ occurred to give benzoamidyl radical **29A**, with the concurrent rege-



Scheme 27 Proposed reaction mechanism



Scheme 28 Visible-light-driven [3+2]/[4+2] annulation reactions of alkenes with *N*-aminopyridinium salts

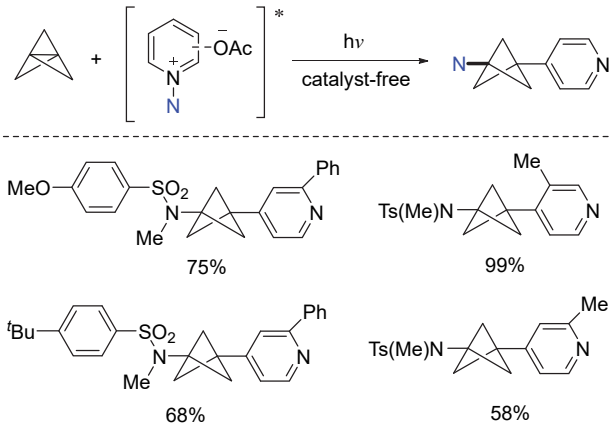


Scheme 29 Proposed reaction mechanism

neration of a [Ir^{IV}] species. Then benzoamidyl radical **29A** adds to the alkene to generate carbon radical **29B**. Subsequently oxidation of carbon radical **29B** to carbocation **29C** by [Ir^{IV}] or radical cyclization of **29C** to deliver radical **29D** occurs. Finally, dihydrooxazole and dihydroisoquinolinone are generated from **29C** and **29D**, respectively.

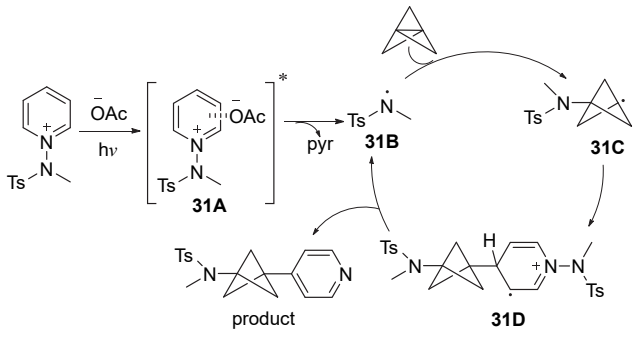
3 React with alkane

Through the formation of electron donor acceptor (EDA) complexes, the [1.1.1]propellants (BCP) were aminopyridinated with *N*-aminopyridine salts as bifunctional reagents. This method enables amino and pyridine groups directly to install on the bicyclic [1.1.1]pentane framework without external photocatalyst (Scheme 30).[18] In addition, the strategy is also extended to P-centered free radicals and CF_3 free radicals, which cross the BCP core in an unprecedented way with *N*-aminopyridine salts in the form of three-component coupling. This reaction offers a convenient and powerful synthetic tool for accessing 1,3-aminopyridylated BCPs while controlling the C4-selectivity of the pyridine ring.



Scheme 30 1,3-Aminopyridylation of [1.1.1]propellane with *N*-aminopyridinium salts

Control experiments imply that the reaction pathways proceed in the proposed stepwise process. The plausible mechanism of the current method is illustrated in Scheme 31.[18] Initially, a small quantity of photoexcited EDA complex **31A** undergoes a SET reaction via irradiation with blue LEDs to yield electrophilic amidyl radical **31B**. Subsequently, the resulting amidyl radical is trapped by the propellane to provide BCP-radical intermediate **31C** via cleavage of the central σ-bond. Subsequently, the BCP radical **31C** adds regioselectively to the C4 position of another *N*-aminopyridinium salt to generate intermediate



Scheme 31 Proposed reaction mechanism

31D. Next, the final product is formed from the resulting cationic radical species **31D** via deprotonation and cleavage of the N—N bond, along with the release of amidyl radical **31B**. Experiment of light-dark cycle and the measured quantum yield (Φ=2.7) were conducted, indicating the radical chain propagation mechanism was possible.

4 Conclusion

The recent advances of pyridinium salt serves as a powerful nitrogen radical precursor in visible light-induced reactions are summarized. In the presence of visible light and photocatalyst, pyridinium salts easily undergo single electron reduction and N—N bond fragmentation to deliver N radicals. Then various N radicals participated reactions could occurred and provided the desired products. Although great progress has been made in this area, there are some challenges needed to be addressed. The substrate scope is not wide enough. More types of substrate should be tried. For example, the visible light induced reaction of pyridinium salts with alkynes is desirable. The reaction mechanism needs further research, which can help us better predict and design new reactions. Additionally, the asymmetric radical reaction involving *N*-amino pyridine salts also deserves further study. It is believed that more and more related works will be published in the near future.

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