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Metal-Free Amino(hetero)arylation and Aminosulfonylation of Alkenes Enabled by Photoinduced Energy Transfer

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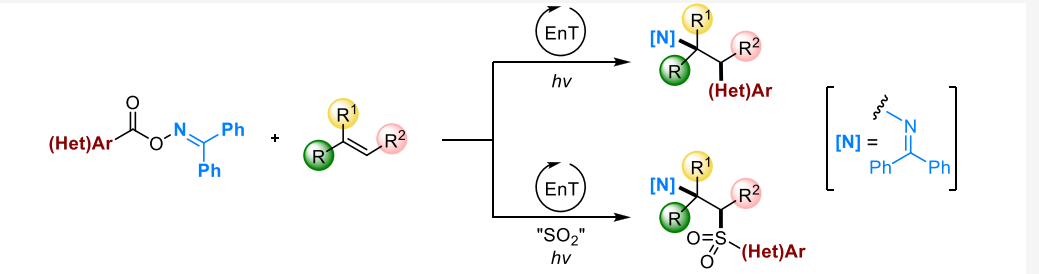

ABSTRACT: β-(Hetero)arylethylamines are privileged structural motifs found in many high-value organic molecules, including pharmaceuticals and natural products. To construct these important molecular skeletons, previous methods are mainly achieved by amino(hetero)arylation reaction with the aid of transition metals and preactivated substrates. Herein, we report a metal-free and photoinduced intermolecular amino(hetero)arylation reaction for the single-step installation of both (hetero)aryl and iminyl groups across alkenes in an efficient and regioselective manner. This method shows broad scope (up to 124 examples) and excellent tolerance of various olefins—from the simplest ethylene to complex multisubstituted alkenes can all participate in the reaction. Furthermore, aminosulfonylation of alkenes can be also conducted in the presence of sodium bisulfite as the SO_2 source.

1. INTRODUCTION

The β-(hetero)arylethylamine scaffold is a key pharmacophore in many biologically active natural products and pharmaceuticals that accomplishes a wide range of important functions.[1] Scheme 1A has shown some representative organic molecules containing β-(hetero)arylethylamine core structures with various pharmacological activities. Thus, their importance as medicinally privileged functionalities has motivated the development of effective synthetic methods to access this structural motif in a rapid and diverse manner. Among the currently developed methods toward the synthesis of β-(hetero)arylethylamine units, transition-metal-catalyzed alkene amino(hetero)arylation is generally regarded as one of the most efficient and straightforward strategies, which enables a series of intramolecular transformations to proceed for the preparation of diverse nitrogen heterocycles.[2] Despite the effectiveness of intramolecular reaction modes, intermolecular variants have gained limited success and been significantly restricted by the requirement of suitable directing groups on the alkenes or arenes.[3]

In recent years, the development of visible light photocatalysis has witnessed substantial progress on the constructive difunctionalization of alkenes.[4] Within this framework, several elegant synthetic strategies have been devoted to the development of intermolecular alkene amino(hetero)arylation reactions via radical pathways.[5] For example, Stephenson and co-workers reported that arylsulfonylacetamides can serve as bifunctional reagents for amidoarylation of electron-rich styrenes via a photocatalytic pathway (Scheme 1B, *i*).[6] In contrast to Stephenson's method that targets single-electron oxidation of alkenes, the groups of Studer, Hong, Molander, Chu, and others reported a different type of reaction approach that generates reactive *N*-centered radical species that then react with alkenes, followed by trapping with (hetero)arenes to give the β-(hetero)arylethylamine products (Scheme 1B, *ii*).[7] In order to reach different regioselectivities of alkene amino(hetero)arylation, a third type of reaction was achieved by the photochemical formation of (hetero)aryl radicals. After (hetero)aryl radical addition across alkenes, a Ritter-type reaction or copper-catalyzed azido-group transfer process occurred to release functionally diverse β-arylethylamines

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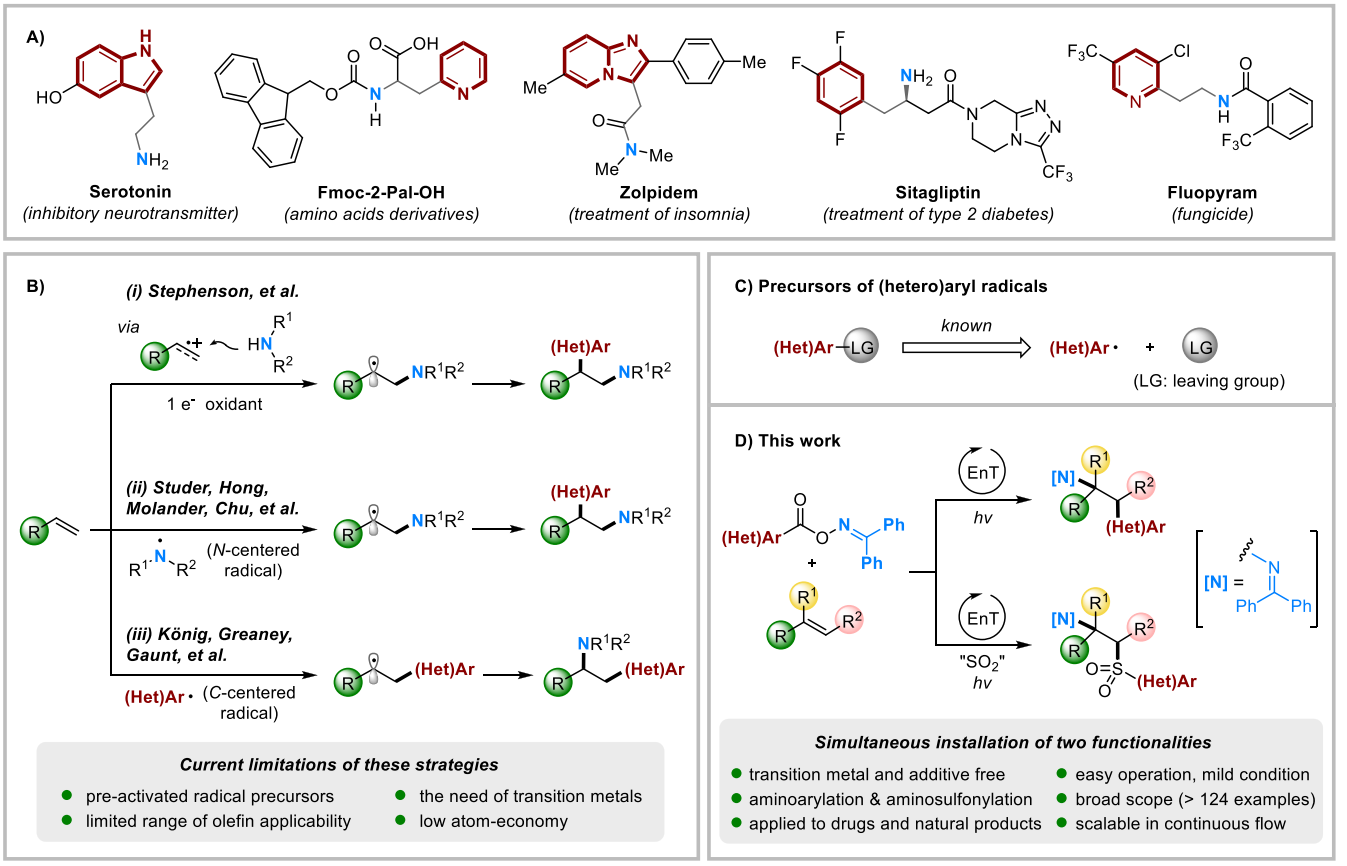
Scheme 1. Current Status for Alkene Amino(hetero)arylation and Our Reaction Design



(Scheme 1B, *iii*).[8] Despite the advantages demonstrated by these radical-mediated transformations, the requirement of preactivated precursors, the limited range of olefin applicability, and the low atom-economy have restricted their wider applications. Furthermore, considering that *β*-(hetero)arylethylamine derivatives are mainly utilized in the pharmaceutical industry, it is mandatory to remove toxic trace metal contaminants from products when using transition metals as catalysts. Therefore, metal-free and sustainable protocols for alkene amino(hetero)arylation reaction without preactivation is highly desirable.

The ubiquity of heterocycles in pharmaceuticals and agrochemicals has demonstrated the significance of these motifs in organic synthesis.[9] With the advent of visible light catalysis, it is of great significance to construct *β*-(hetero)arylethylamine derivatives directly from aryl and heteroaryl radicals.[10] To date, a variety of preactivated (hetero)aryl radical precursors have been well exploited,[11] including (hetero)aryl diazonium salts,[12] di(hetero)aryliodonium salts,[13] triflates,[14] oxime esters,[15] and *N*-hydroxyphthalimide (NHP) esters.[16] Another route is to utilize stable and commercially available substrates as radical precursors, such as (hetero)aryl halides,[17] carboxylic acids,[18] and sulfonyl chlorides.[19] Although continuous progress has been made in research, to the best of our knowledge, all reported radical precursors are designed and utilized to install only single and undifferentiated (hetero)aryl functionalities (Scheme 1C). To achieve a more challenging amino(hetero)arylation, we considered whether a simple bifunctional reagent could be well designed that is capable, in principle, of simultaneously generating both (hetero)aryl and nitrogen radicals but with different reactivity. If successful, highly regioselective addition of the (hetero)aryl radicals to alkenes, along with the subsequent radical−radical coupling, could lead to the valuable *β*-(hetero)arylethylamine core structures in a single step.

Recent advances in visible light photocatalysis have already demonstrated that the use of a bifunctional reagent via triplet energy transfer provides a facile and straightforward route to vicinal alkene difunctionalization.[20] Herein, we report the successful validation of oxime ester-based and bifunctional (hetero)aryl radical precursors that are utilized for the simultaneous generation of a nucleophilic (hetero)aryl radical and an ambiphilic iminyl radical via an energy transfer (EnT) pathway, thereby providing a rapid and versatile protocol for amino(hetero)arylation of alkenes (Scheme 1D). Noteworthy features of this study include the following: (1) Without the participation of any transition metals, the use of cheap and commercially available 2-*i*Pr-thioxanthone (**2-*i*PrTX**) as an organic photosensitizer, as well as mild reaction conditions, simple operation, scalability, and efficient flow reaction, proves that the method has great potential for industrial application. (2) This method showed a very wide scope of substrates (up to 124 examples) and excellent tolerance to diverse alkenes—from the simplest ethylene to complex multisubstituted alkenes, all can participate in the reaction, that is, without the restriction of electronic properties of olefins and steric hindrance of substituents. (3) Importantly, precursors of (hetero)aryl radicals, including pyridine, quinoline, pyrimidine, pyrazine, thiophene, and thiazole, are suitable for this reaction, and even phenyl radicals can smoothly react with alkenes to form *β*-arylethylamine derivatives. (4) Through the introduction of sodium bisulfite ($NaHSO_3$) as a SO_2 surrogate,

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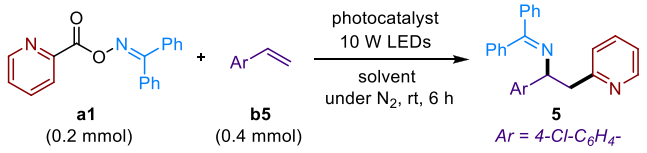
aminosulfonylation can be also achieved, which greatly expands the applicable range of β-aminosulfone derivatives.

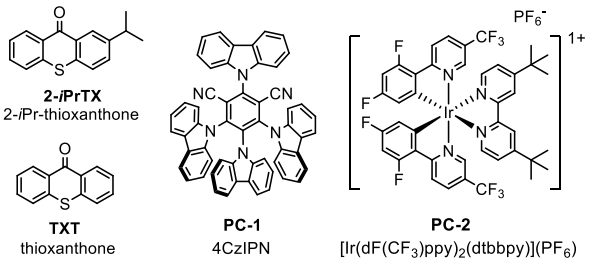
2. RESULTS AND DISCUSSION

Our investigation commenced with the exploration of a suitable bifunctional reagent, in principle, for making both pyridine radicals and amine radicals simultaneously but with different reactivities. With this aim in mind, we selected a simple and stable oxime ester compound (**a1**) as a bifunctional reagent and examined the reactivity of **a1** with styrene **b5** under light irradiation in order to achieve alkene amino(hetero)arylation reaction. As shown in Table 1, it was found

Table 1. Optimization Study[a]



entry	photocatalyst [5 mol %]	wavelength [10 W LEDs]	solvent [0.07 M]	yield **5** (%)[b]
1	**2-*i*PrTX**	405 nm	EtOAc	75
2	**TXT**	405 nm	EtOAc	70
3	**PC-1**	405 nm	EtOAc	58
4	**PC-2**	405 nm	EtOAc	65
5	**2-*i*PrTX**	390 nm	EtOAc	78
6	**2-*i*PrTX**	370 nm	EtOAc	67
7	**2-*i*PrTX**	390 nm	DMSO	50
8	**2-*i*PrTX**	390 nm	$CHCl_3$	53
9	**2-*i*PrTX**	390 nm	DMF	47
10	**2-*i*PrTX**	390 nm	*i*PrOAc	78
11		365 nm	EtOAc	9
12		390 nm	EtOAc	N.D.
13[c]	**2-*i*PrTX**		EtOAc	N.D.
14[d]	**2-*i*PrTX**	390 nm	EtOAc	N.D.



[a]Reaction conditions: **a1** (0.20 mmol, 1.0 equiv), styrene derivative **b5** (0.40 mmol, 2.0 equiv), photocatalyst (0.01 mmol, 5 mol %) in solvent (3.0 mL, 0.07 M) at room temperature, under N_2 atmosphere, 390 nm LEDs (10 W), 6 h. [b]Yields are of isolated products after chromatographic purification. [c]The reaction was performed in the dark. [d]Under air atmosphere.

that the use of 2-*i*Pr-thioxanthone (**2-*i*PrTX**) as the photocatalyst showed the best reaction efficiency compared with other commonly used catalysts, such as thioxanthone (**TXT**), 4CzIPN (**PC-1**), and $[Ir(dF(CF_3)ppy)_2(dtbbpy)](PF_6)$ (**PC-2**) (entries 1−4). Considering that the maximum absorption wavelength of **2-*i*PrTX** is around 405 nm, we also explored other irradiation wavelengths. To our delight, the yield of **5** was increased to 78% by using 5 mol % **2-*i*PrTX** under the irradiation of 390 nm purple LEDs (entry 5), whereas a further decrease of the irradiation wavelength did not improve the yield (entry 6). Further optimizations were carried out by screening a variety of solvents, such as DMSO, $CHCl_3$, and DMF, but they all provided unsatisfying results (entries 7−9). The use of *i*PrOAc gave yields comparable with those of EtOAc (entry 10). In addition, a control reaction performed without the addition of a photosensitizer showed that an inefficient amino(hetero)arylation was still operative under 365 nm irradiation (entry 11), thereby revealing that **a1** can also be directly excited by UV light irradiation. Control experiments finally demonstrated that photosensitizer, light irradiation, and inert atmosphere are all requisite for this transformation (entries 12−14).

2.1. Photocatalytic Amino(hetero)arylation. With the optimized reaction conditions in hand, the scope of this amino(hetero)arylation reaction was systematically investigated by using different olefins. As shown in Scheme 2, a wide range of monosubstituted olefins, including diverse styrene derivatives, electron-rich and electron-deficient alkenes, enynes, and even unactivated alkenes, were all successfully transformed into the 2-pyridylethylamine products in moderate to good yields with excellent regioselectivity. First, various styrene derivatives with different electron-donating, as well as electron-withdrawing groups, at the *para*-position of the aromatic ring underwent this amino(hetero)arylation reaction smoothly to produce the corresponding products in 52−78% yields (**1**−**8**), and the structure of **1** was characterized by X-ray crystallographic analysis (CCDC 2252837).[21] Polysubstituted 2,3,4,5,6-pentafluorostyrene was also well tolerated, as shown by the formation of the corresponding product **9** in 63% yield. Other terminal aryl alkenes, such as 2-vinylnaphthalene, 2-vinylthiophene, and 2-vinylpyridine, could also be applied to deliver products **10**−**12** in 52−64% yields. The scope of electron-rich alkenes bearing different substituents was further explored. Vinyl ethers and enamides could be engaged in this photochemical reaction and showed good reactivity (**13**−**15**). We were also delighted to see that vinyl silane underwent the reaction in the same pathway to give product **16** in 63% yield. It is noteworthy to mention that this catalytic alkene difunctionalization strategy allowed a series of electron-deficient alkenes to proceed well, such as acrylates (**18**), acrylonitriles (**19**), acrylamides (**20**−**23**), vinyl phosphonates (**24**), and polyfluorinated alkenes (**25**). Olefin bearing a boron moiety could deliver the valuable α-amino boronate product **17** in moderate yield, which provides the possibility for further derivatizations.[22] Furthermore, the reactivity of unactivated terminal alkenes was examined under the standard conditions. To our delight, a number of unactivated alkenes that bear diverse functional groups, including alkyl groups, esters, ketones, ethers, silanes, phthalimides, and bromines, were all suitable for this reaction to give the corresponding products in moderate yields (**26**−**35**).

We next sought to explore the scope of 1,1-disubstituted alkenes for the photoinduced alkene amino(hetero)arylation reaction. Similar to the results of monosubstituted olefins, the use of 1,1-disubstituted alkenes also proved to be effective under the standard conditions. Various 1,1-disubstituted alkenes with monosubstituted aromatics (electron-withdrawing or electron-donating groups) and polysubstituted aromatics, as well as substrates containing exocyclic olefins, smoothly underwent amino(hetero)arylation in moderate to excellent yields (**36**−**44**). Interestingly, 1,3-enynes were tolerated, with good compatibility for both terminal and internal acetylene, which were capable of generating the desired β-alkynyl-substituted 2-pyridylethylamines with exclusive chemo- and

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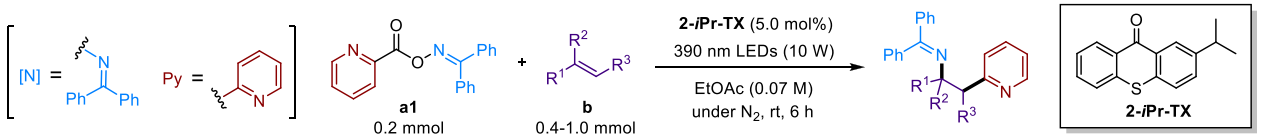
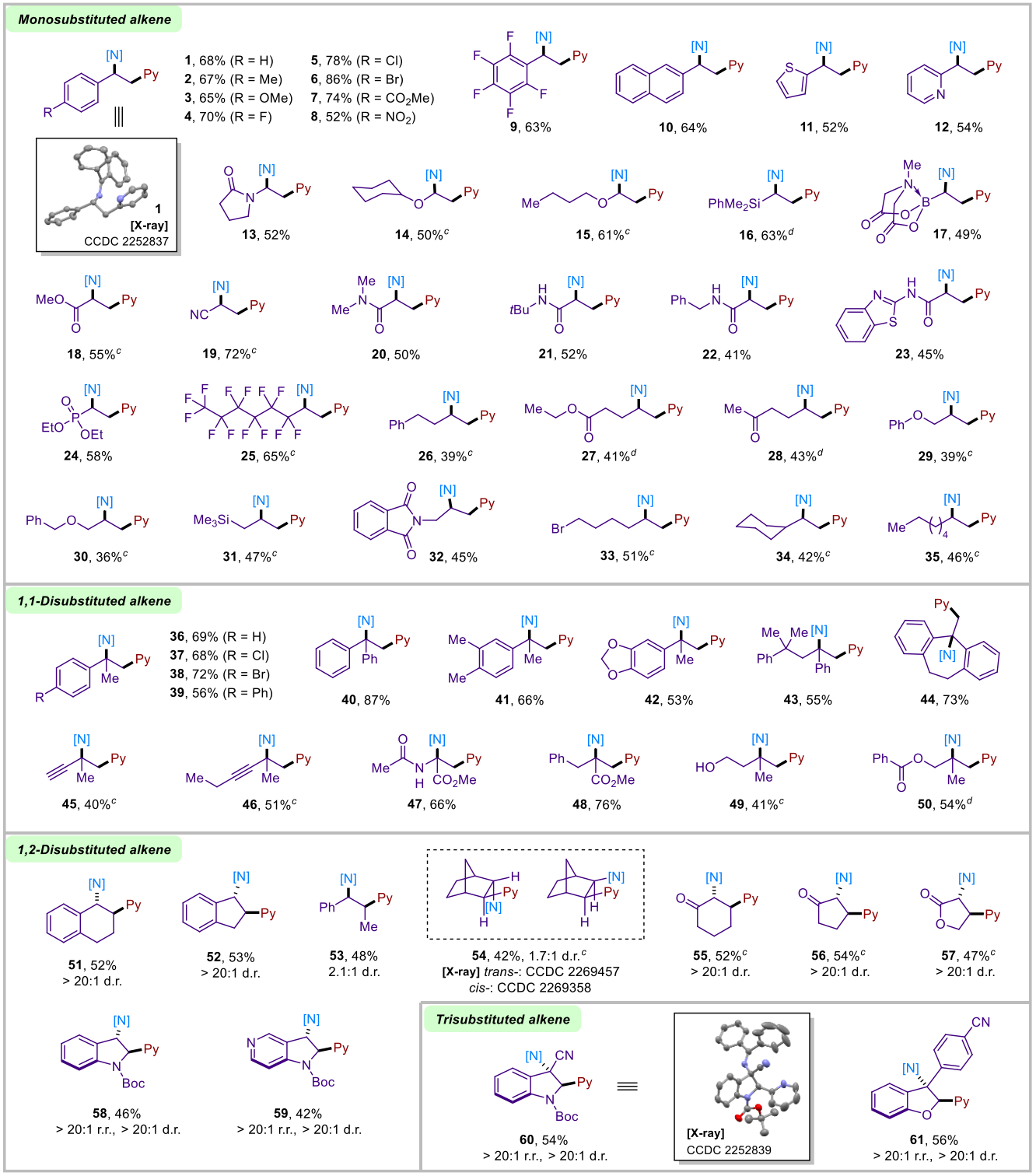
Scheme 2. Substrate Scope of Alkene[a,b]





[a]Reaction conditions: **a1** (0.20 mmol, 1.0 equiv), **b** (0.40 mmol, 2.0 equiv), 2-*i*Pr-thioxanthone (0.01 mmol, 5 mol %), 10 W 390 nm LEDs, under N_2 atmosphere, rt in ethyl acetate (3.0 mL, 0.07 M) for 6 h. [b]Yields of isolated products. [c]Substrate **b** (1.0 mmol, 5.0 equiv) was utilized. [d]Substrate **b** (0.6 mmol, 3.0 equiv) was used. Regioselectivity (rr) and diastereoselectivity (dr) were determined by ^{1}H NMR analysis.

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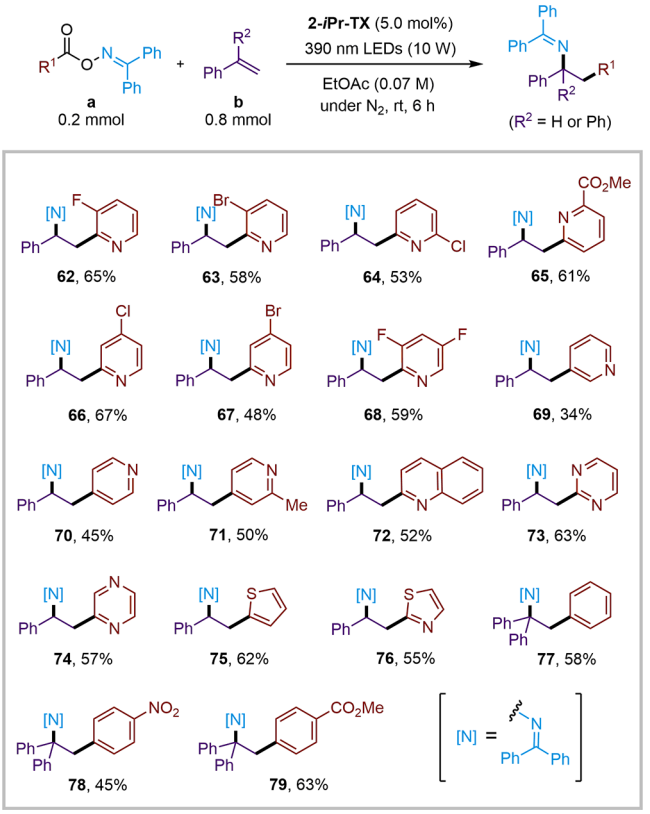
regioselectivity (**45**, **46**). Electron-deficient and unactivated 1,1-disubstituted alkenes were also suitable for this transformation, which gave **47**−**50** in moderate to good yields.

In comparison with terminal olefins, 1,2-disubstituted alkenes are more sterically hindered and show weaker reactivity in radical-mediated addition reactions. However, in our reaction system, either symmetrical or unsymmetrical 1,2-disubstituted alkenes could successfully deliver the desired alkene difunctionalization products in satisfactory yields and diastereoselectivities (**51**−**57**). Notably, exclusive regioselectivity of our amino(hetero)arylation reaction was afforded, with amination observed at the benzylic site (**51**−**53**) or the carbonyl α-position (**55**−**57**). This is because the regioselectivity is largely affected by the stability of radical intermediates after the addition of pyridyl radicals to alkenes. The reaction of bicyclo[2.2.1]hept-2-ene under standard conditions gave two major isomers with 1.7:1 dr (**54**, *trans*-/*cis*-), the configurations of which were both determined by X-ray crystallographic analysis (CCDC 2269457 and 2269358).[21] (Hetero)arenes, such as indoles and benzofurans, widely exist in natural products and show important application value. Despite the presence of potential alkene subunits, these (hetero)arenes are largely limited in radical-mediated difunctionalization reactions because of the inherent low reactivity of aromatic systems. Notably, successful dearomatization of indole skeletons was achieved using our method (**58** and **59**). In addition, C3-substituted indoles and benzofurans smoothly underwent the reaction process to afford the desired products **60** and **61** in 54% and 56% yields, respectively, where the antigeometry between the pyridyl and iminyl functionalities were determined by X-ray crystallographic analysis of **60** (CCDC 2252839).[21]

The scope of the (hetero)aromatic component was further assessed using styrene or 1,1-diphenylethylene as acceptors. Our experimental results revealed that a range of oxime esters could be successfully employed, as shown in Scheme 3. Oxime esters bearing different substituents on the pyridyl group were all converted into the corresponding difunctionalization products in good to moderate yields (**62**−**71**), including substrates containing fluorine (**62**, **68**), bromine (**63**, **67**), chlorine (**64**, **66**), ester (**65**), and methyl moiety (**71**), regardless of whether the substituents were in the *ortho*-, *para*, or *meta*-position. Substrates with 3- or 4-pyridyl moieties proceeded well (**69**, **70**). In addition, quinoline, pyrimidine, pyrazine, thiophene, and thiazole units could also be smoothly transferred from the corresponding oxime esters with styrene in synthetically useful yields (**72**−**76**), which greatly expands the range of applications for (hetero)aryl moiety incorporation. To our delight, the aminoarylation of 1,1-diphenylethylene also proved to be viable through unstable phenyl radicals, which resulted in β-arylethylamine derivatives in 45−63% yields (**77**−**79**).

2.2. Photocatalytic Aminosulfonylation. β-Aminosulfones are important structural motifs in numerous pharmaceuticals and play an important role in organic synthesis.[23] Herein, we successfully achieved the aminosulfonylation of alkenes by utilizing sodium bisulfite ($NaHSO_3$) as a SO_2 surrogate to react with oxime esters and alkenes. Compared with reactions of aryl sulfonyl radicals, the use of heteroaromatic sulfonyl radicals has been less reported to date, probably because of the high costs and difficulties in preparing heteroaryl sulfonyl radical precursors. As shown in Scheme 4, under the standard reaction conditions, a wide

Scheme 3. Substrate Scope of (Hetero)aryl Radical Precursor[a,b]



[a]Reaction conditions: **a** (0.20 mmol, 1.0 equiv), **b** (0.40 mmol, 2.0 equiv), 2-*i*Pr-thioxanthone (0.01 mmol, 5 mol %), 10 W 390 nm LEDs, under N_2 atmosphere, rt in ethyl acetate (3.0 mL, 0.07 M) for 6 h. [b]Yields of isolated products.

range of alkenes, which includes styrenes, 2-vinylnaphthalene, 2-vinylpyridine, and cyclic alkenes, reacted well with **a1** to provide β-aminosulfone derivatives in moderate to good yields and with excellent regioselectivity (**80**−**89**). The scope of the (hetero)aryl component was also evaluated using styrene as acceptor. Substituents on (hetero)aryl moieties could be combined with alkyl units, halogens, and ester groups at *ortho*, *meta*, and *para* sites (**90**−**96**). Moreover, oxime esters that can release pyrimidine (**97**), phenyl (**98**), and alkyl radicals (**99**, **100**) upon light irradiation also proved to be viable substrates for our reaction system.

2.3. Synthetic Applications. Late-stage modification of complex organic molecules is the basis for the evaluation of a practical protocol. The direct use of oxime esters **a1** with complex alkene substrates to construct β-(hetero)-arylethylamine units makes the standard photochemical conditions applicable for the late-stage modification of several biologically valuable natural products and pharmaceuticals (Scheme 5A). Two α-amino acid derivatives, D-phenylalanine and D-alanine derivatives, were both able to react with **a1** to form the corresponding β-(hetero)arylethylamine-containing products (**101**, **102**). Naturally derived compounds that are widely used in the pharmaceutical industry, such as citronellol (**103**), (−)-menthol (**104**), phytol (**107**), perillol (**109**), and diprogulic acid derivatives (**111**), were also effectively transformed into β-(hetero)arylethylamine units in moderate to good yields. Moreover, D-glucose and vitamin E derivatives,

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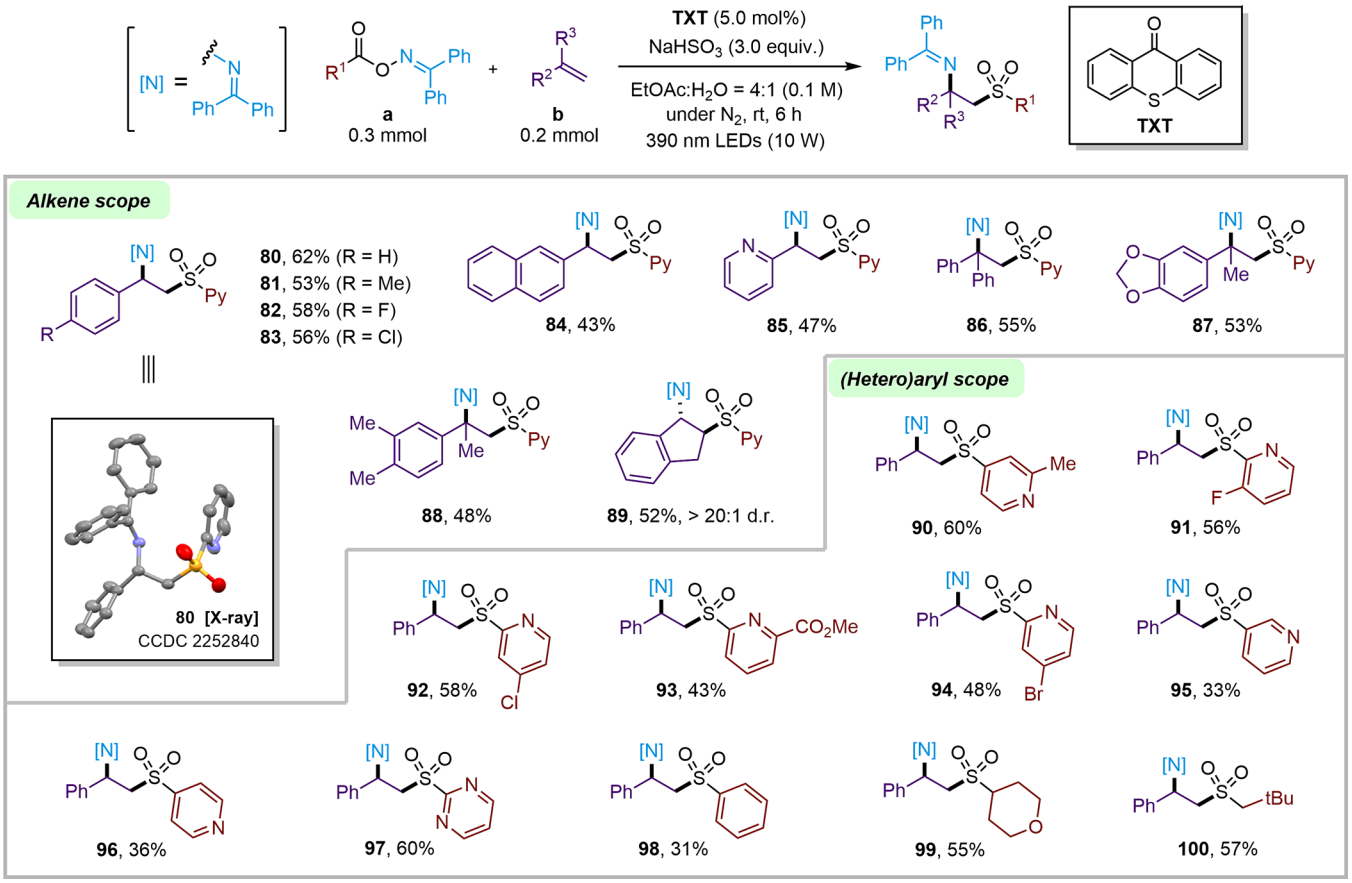
Scheme 4. Substrate Scope for Aminosulfonylation of Alkene with Oxime Ester and $NaHSO_3$[a,b]



[a]Reaction conditions: **a** (0.30 mmol, 1.5 equiv), **b** (0.20 mmol, 1.0 equiv), $NaHSO_3$ (0.60 mmol, 3.0 equiv), thioxanthone (0.01 mmol, 5 mol %), 10 W 390 nm LEDs, under N_2 atmosphere, rt in ethyl acetate/H_2O = 4:1 (2.0 mL, 0.1 M) for 6 h. [b]Yields of isolated products.

which are both important to human health, were successfully employed and gave **102** and **108** in 52% and 66% yields, respectively. Molecular drug derivatives, including fenofibrate (**105**), piribedil (**110**), and oxaprozin (**112**), reacted smoothly to generate the desired difunctionalization products in 46−67% yields. We further explored the viable oxime esters bearing complex structural motifs to undergo photocatalytic aminosulfonylation reaction. The use of oxime esters containing (1*S*)-(−)-camphanic acid and gemfibrozil units successfully delivered the desired sulfone products **113** and **114** in 62% and 57% yields, respectively, in the presence of styrene and sodium bisulfite under the standard conditions.

In order to investigate the regioselectivity of our method, we further employed olefin substrates **b74** and **b75** that both contain two different types of carbon−carbon double bonds in their structures (Scheme 5B). The photochemical reaction of **b74** or **b75** with oxime ester **a1** revealed that amino(hetero)arylation preferentially occurred at the more reactive electron-deficient alkenes rather than the unactivated ones, thereby giving the corresponding products **115** and **116** in 46% and 55% yields, respectively.

To highlight the synthetic utility of this methodology, product derivatization reactions were subsequently performed (Scheme 5C). Imine compounds from either amino(hetero)arylation (**1**) or aminosulfonylation (**118**) were readily deprotected by the use of pyridinium *p*-toluenesulfonate (PPTS) under mild conditions to give the corresponding unprotected primary amines (**117**, **118**),[24] thereby facilitating the downstream transformation. In order to further illustrate the synthetic potential, we conducted a gram-scale continuous flow reaction using oxime ester **a1** as a substrate to react with acrylonitrile **b19**. Through the application of a flow rate of 2 $mL·min^{-1}$ and a residence time of 6 h, we were able to scale up the amino(hetero)arylation reaction by 30-fold (6.0 mmol). The collected solution, after workup and purification, afforded the corresponding difunctionalization product **19** in a 68% yield (1.26 g).

In addition, this protocol offers general access to α-amino acids by treating compound **19** with 6 M HCl under heating conditions to produce α-amino acid **119** in 89% yield. Alternatively, treatment of **19** with PPTS at room temperature generated valuable α-amino nitrile compound **120** in 91% yield. After the successful validation of photoinduced amino(hetero)arylation with diverse alkenes, we envisioned that ethylene may also be utilized in our developed protocol, as ethylene is the simplest alkene and about 170 million tons of it are produced annually worldwide, which far exceeds that of any other organic compounds.[25] However, because of its inherent simplicity and concerns about handling this flammable gas, ethylene has rarely been utilized in a radical-mediated conversion process without the need for high pressure. It is noteworthy to mention that a mixture of ethylene (1.0 bar) and oxime ester **a1** was found to be efficiently converted into the corresponding difunctionalization product **121** in moderate yield, which greatly highlighted the application potential of our method.

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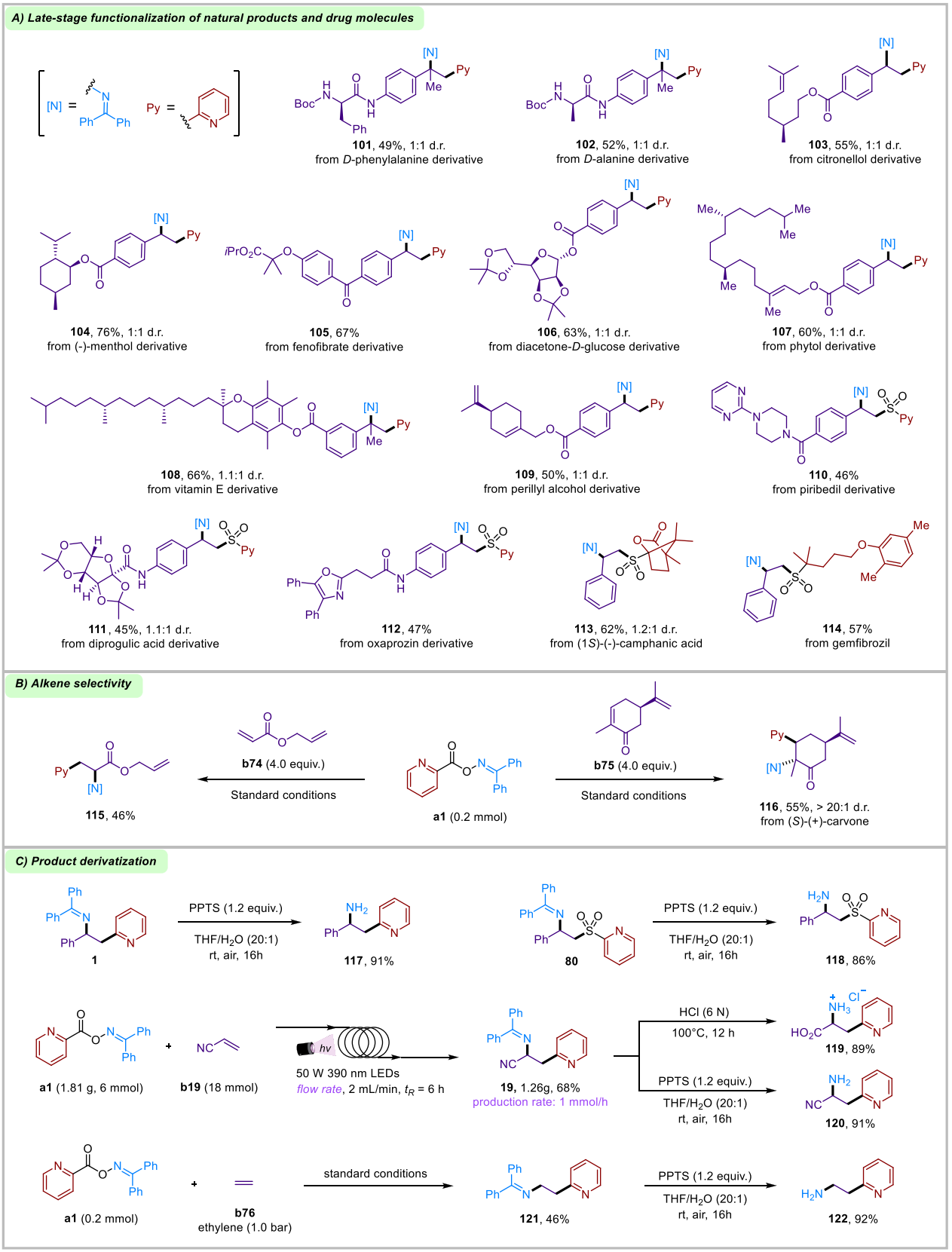
Scheme 5. Synthetic Application



2.4. Mechanistic Study. To gain more mechanistic insights into the amino(hetero)arylation and aminosulfonylation reactions, a series of mechanistic experiments were conducted, as shown in Scheme 6. Initially, the photochemical reaction of **a1** with styrene was completely inhibited by the addition of 2.0 equiv of 2,2,6,6-tetramethylpiperidinooxy (TEMPO) as a radical scavenger (Scheme 6A), which suggested the radical nature of the transformation. Moreover,

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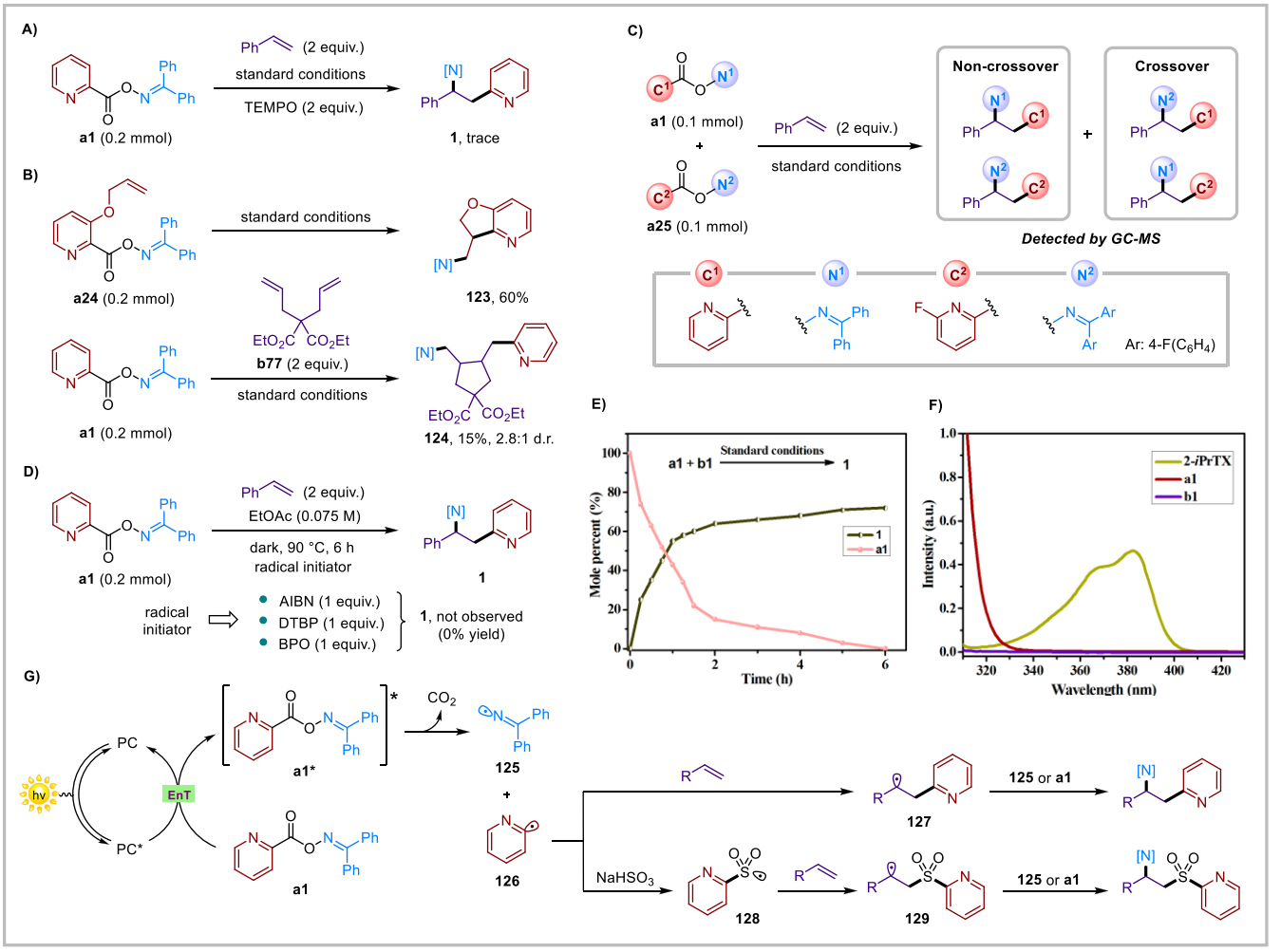
Scheme 6. Mechanistic Study



the involvement of both pyridyl and iminyl radicals was identified by the formation of compound **123** through 5-*exo*-trig radical addition/cyclization, as well as by the ring-closing reaction of **a1** with diene **b77** (Scheme 6B). Subsequently, the formation of crossover products was detected by GC-MS analysis in a radical crossover study of oxime esters **a1** and **a25** with styrene, which explained the occurrence of the radical−radical cross-coupling step outside the solvent cage and verified the presence of both pyridyl and iminyl radicals in the reaction system (Scheme 6C). Instead of using photosensitizer, the addition of commonly used radical initiators, such as 2,2′-azobis(2-methylpropionitrile) (AIBN),[26a] di-*tert*-butyl peroxide (DTBP),[26b,c] and benzoyl peroxide (BPO),[26d] cannot initiate the difunctionalization reaction under heating conditions (Scheme 6D), which indicates that photoinduced conditions in the presence of photosensitizer are significant for the production of both pyridyl and iminyl radicals, as well as the following radical addition process. Furthermore, the longer lifetime of *N*-centered iminyl radical can be inferred by the observation of all probable N−N dimeric species by GC-MS.[21] The kinetic profile of a standard reaction mixture of **a1** with **b1** showed that the reaction proceeded very fast and did not have obvious induction periods, with the majority of the product formed within 1 h (Scheme 6E). UV−vis absorption spectroscopy further confirmed that the photosensitizer 2-*i*Pr-thioxanthone (**2-*i*PrTX**) is the only light-absorbing species in the reaction mixture near the excitation wavelength (λ_{max} = 390 nm, Scheme 6F). These results implied that an energy transfer (EnT) process is likely to occur in the reaction process.

The quantum yields for the amino(hetero)arylation and aminosulfonylation reactions were determined to be 2.5 and 1.4, respectively, which suggests that a free radical chain mechanism may play a role in the reactions.[21] On the basis of the above mechanistic exploration and previous reports,[20i,m] a plausible mechanism is proposed as outlined in Scheme 6G. The reaction starts with an interaction between **a1** and the excited 2-*i*Pr-thioxanthone (**2-*i*PrTX**) through a photoinduced EnT process to generate the excited species **a1***. Then, **a1*** undergoes N−O bond fragmentation to form a persistent iminyl radical and a transient pyridyl radical (species **125** and **126**), together with the release of CO_2. Considering the persistent radical effect of iminyl radical,[27] the pyridyl radical **126** is initially captured by alkene (**b**) at the C2 position to produce transient carbon-centered radical **127**. Finally, the carbon-centered radical intermediate **127** reacts with **125** or **a1** to provide the desired *β*-(hetero)arylethylamine derivatives. In the presence of sodium bisulfite ($NaHSO_3$) as the sulfur dioxide source, the pyridyl radical could be captured by the in situ generated SO_2 to provide a sulfonyl radical intermediate (**128**). Subsequent radical addition of sulfonyl radical **128** with alkene **b** would afford the carbon-centered radical intermediate

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129, which is then reacted with **125** or **a1** to provide the desired β-aminosulfone products.

3. CONCLUSION

In summary, a photoinduced metal-free amino(hetero)-arylation strategy for the rapid conversion of alkene feedstocks into valuable β-(hetero)arylethylamine core structures has been described. The mild reaction conditions, operational simplicity, scalability, and efficient flow reaction demonstrate that the method has great potential for further industrial application. A wide range of substrates (up to 124 examples), from simple ethylene to complex multisubstituted alkenes, can be applied to the reaction. Most importantly, (hetero)aryl radical precursors, including quinoline, pyrimidine, pyrazine, thiophene, and thiazole, are all suitable for this reaction, and even aryl radical can react to form β-arylethylamine derivatives. In addition, by introducing a source of sulfur dioxide (SO_2), aminosulfonylation can also be achieved, which greatly expands the applicable range of β-aminosulfone derivatives. We believe that this method opens up a new synthetic strategy and finds a direct route for the preparation of β-(hetero)-arylethylamines and β-aminosulfones, thereby offering enormous opportunities for selectively installing valuable functional groups across alkenes at the late stage of drug molecule modification. Further development of new photochemical transformations is still underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.3c04073.

Experimental procedures and characterization data for new compounds (PDF)

Accession Codes

CCDC 2252837, 2252839−2252840, 2269358, and 2269457 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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