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Palladium-Catalyzed Cascade Annulation/Allylation of Alkynyl Oxime Ethers with Allyl Halides: Rapid Access to Fully Substituted Isoxazoles

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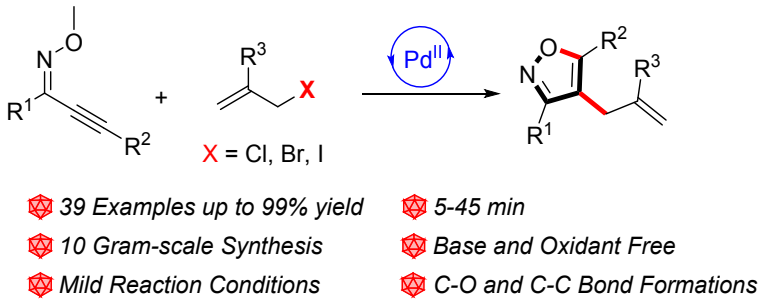


Abstract: A novel and efficient approach for the synthesis of functionalized isoxazoles *via* palladium-catalyzed cascade annulation/allylation of alkynyl oxime ethers with allyl halides has been established. The present protocol exhibits mild reaction conditions, good functional group compatibility, and convenient operation. Moreover, the scalability was performed and further decoration of the isoxazole product was achieved.

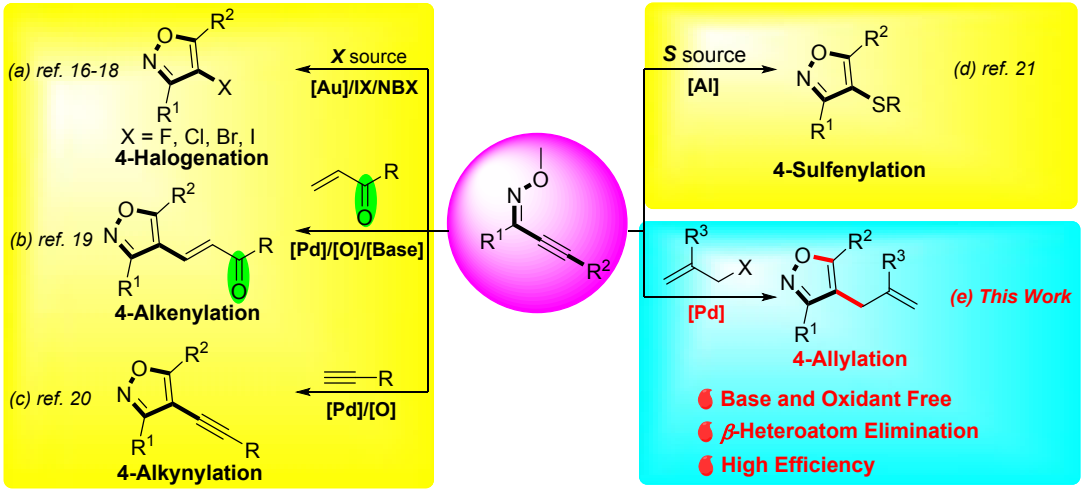
INTRODUCTION

Palladium-catalyzed coupling reaction has attracted substantial attention mainly due to its ability for efficient and straightforward construction of carbon-carbon or/and carbon-heteroatom bonds.[1] As an important chemical transformation type, nucleopalladation of unsaturated hydrocarbons such as halopalladation,[2] aminopalladation,[3] and oxypalladation,[4] has been established in recent years, which can undergo different quenching manners to break the carbon-palladium bond and generate diverse useful frameworks. In particular, the nucleopalladation of alkynes[5] affords a highly reactive and crucial alkenylpalladium intermediate, which can be captured by the activated alkenes,[6] carbon monoxide,[7] allenes,[8] enols[9] and other participants,[10] providing the corresponding alkyl-Pd intermediates. Classically, there are three main approaches applied to quench the alkyl-Pd species: (i) β-H elimination to give an alkene; (ii) β-heteroatom elimination also to afford an alkene; (iii) reductive elimination to generate a saturated C-X bond. Among them, β-heteroatom elimination has been typically investigated in the past few years. For example, Ma and co-workers developed an elegant protocol for the palladium-catalyzed cyclization reaction of 2,3-allenoic acids with ω-1-alkenyl halides for the construction of β-alkyl-substituted butenolides.[11] In 2011, Zhu's group reported the first palladium-catalyzed haloallylation reaction of alkynyl halides to generate various (1*E/Z*)-1,2-dihalo-1,4-dienes.[12] Despite many significant advances in this field, most approaches suffer from some limitations, such as limited substrate scope, low efficiency and regioselectivity issues. Therefore, the development of convenient and

practical synthetic methods under mild reaction conditions for the rapid and straightforward assembly of highly functionalized frameworks is still highly desirable.

Isoxazole architectures represent a privileged scaffold extensively found in many pharmaceutical agents and naturally occurring molecules.[13] Specially, highly substituted isoxazoles exhibit remarkable biological and therapeutic activities, such as antinociceptive, antimicrobial, antibiotic, anti-inflammatory, and anticancer activities.[14] Many representative synthetic methods have been developed for building this heterocyclic moiety in recent years.[15] Among them, cyclization of alkynyl oxime ether has aroused much attention which is summarized in Scheme 1. Ryu[16], Larock[17] and Ruchirawat[18] *et al.* utilized electrophilic cyclization of alkynyl-*O*-methyl oximes for the synthesis of 4-haloisoxazoles, respectively (Scheme 1, a). Chen[19] and our group[20] developed the palladium-catalyzed coupling between alkynyl-*O*-methyl oximes with activated alkenes/alkynes for the construction of 4-alkeny/alkyny isoxazoles (Scheme 1, b and c). Recently, Yang and co-workers[21] have reported the synthesis of 4-sulfenyl isoxazoles *via* $AlCl_3$-mediated electrophilic cyclization/sulfenylation of 2-alkyn-1-one *O*-methyloximes (Scheme 1, d). It is noteworthy that the allyl moiety can improve their biological activities compared to the non-allyl heterocyclic compounds.[22] In 2010, Miyata and co-workers introduced C4 allyl groups into the preformed isoxazoles *via* the gold-catalyzed intramolecular domino cyclization and Claisen-type rearrangement reaction.[23] Based on our continuous interest in nucleopalladation of alkynes,[24] herein, we disclose a palladium-catalyzed cascade cyclization/alkylation of alkynes with alkenes for the

synthesis of 4-allylisoxazole derivatives (Scheme 1, e). This protocol provides quick access to diverse polyfunctionalized isoxazoles from readily available starting materials, which should have potential applications in synthetic and pharmaceutical chemistry.



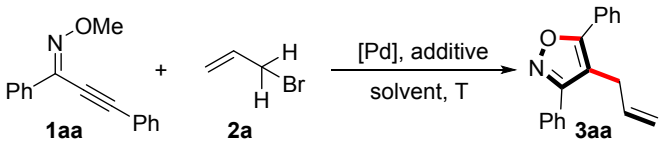
Scheme 1. Representative Methods for the Synthesis of 4-Functionalized Isoxazoles from Alkynyl Oxime Ethers

RESULTS AND DISCUSSION

Functionalized alkyne (**1aa**) and allyl bromide (**2a**) were selected as the model substrates to screen the optimal conditions for this cascade protocol. As summarized in Table 1, we initially used $PdCl_2$ as the catalyst, and *n*-Bu_4NI as the additive in DMF at 80 °C, while a trace amount of allylated product **3aa** was detected by GC-MS after 3 h (entry 1). Additive screening revealed that *n*-Bu_4NBr was a suitable choice, affording the desired product **3aa** in 40% yield. However, other additives including *n*-Bu_4NCl, NaBr and KBr were less effective (entries 2, 4 and 5). $Pd(OAc)_2$ was found to be better than other Pd catalysts such as $PdCl_2$ or $Pd(TFA)_2$ (entries 6 and 7).

Investigation of different solvents showed that DMF was the optimal solvent for this reaction (entries 8-14), and product **3aa** could be isolated in 95% yield when using $Pd(OAc)_2$ as the catalyst and DMF as the solvent (entry 6). Satisfyingly, reaction time optimization revealed that this transformation could be finished in 20 min (entry 15). It is noted that when the reaction was performed with only 3 mol % of Pd catalyst, the desired product **3aa** was still detected in 98% yield (entries 16-18). Further reaction condition optimizations revealed that either decreasing or increasing the temperature led to a negative effect on the product yield (entries 19-21). Control experiments indicated that Pd catalyst and additive (*n*-Bu_4NBr) were necessary for this tandem reaction (entries 22 and 23). Notably, under N_2 atmosphere the reaction could be performed successfully using $Pd(OAc)_2$ as catalyst (entry 24). No reaction occurred when Pd^0 catalyst such as $Pd(PPh_3)_4$, $Pd(PCy_3)_2$ and $Pd_2(dba)_3$ was used (entries 25-27). Thus, the optimal conditions for this transformation was defined as follows: $Pd(OAc)_2$ (3 mol %) as catalyst, *n*-Bu_4NBr (1.0 equiv) as additive, DMF (1.0 mL) as solvent at 80 °C for 20 min.

Table 1. Optimization of Reaction Conditions[a]



Entry	Catalyst	Additive	Solvent	T (°C)	Yield (%)[b]
1	$PdCl_2$ (10)	*n*-Bu_4NI	DMF	80	trace
2	$PdCl_2$ (10)	*n*-Bu_4NCl	DMF	80	20
3	$PdCl_2$ (10)	*n*-Bu_4NBr	DMF	80	40 (37)

4	$PdCl_2$ (10)	NaBr	DMF	80	trace
5	$PdCl_2$ (10)	KBr	DMF	80	trace
6	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	DMF	80	98 (95)
7	$Pd(TFA)_2$ (10)	*n*-Bu_4NBr	DMF	80	80 (78)
8	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	Toluene	80	trace
9	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	NMP	80	trace
10	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	DMSO	80	trace
11	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	DCE	80	trace
12	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	CH_2Cl_2	80	trace
13	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	CH_3CN	80	47
14	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	CH_3NO_2	80	trace
15[c]	$Pd(OAc)_2$ (10)	*n*-Bu_4NBr	DMF	80	98 (95)
16[c]	$Pd(OAc)_2$ (5)	*n*-Bu_4NBr	DMF	80	98 (95)
17[c]	**$Pd(OAc)_2$ (3)**	***n*-Bu_4NBr**	**DMF**	**80**	**98 (95)**
18[c]	$Pd(OAc)_2$ (2)	*n*-Bu_4NBr	DMF	80	80 (78)
19[c]	$Pd(OAc)_2$ (3)	*n*-Bu_4NBr	DMF	100	90 (88)
20[c]	$Pd(OAc)_2$ (3)	*n*-Bu_4NBr	DMF	70	72 (70)
21[c]	$Pd(OAc)_2$ (3)	*n*-Bu_4NBr	DMF	50	50
22[c]	-	*n*-Bu_4NBr	DMF	80	n.r.
23[c]	$Pd(OAc)_2$ (3)	-	DMF	80	n.r.
24[c, d]	$Pd(OAc)_2$ (3)	*n*-Bu_4NBr	DMF	80	98 (95)
25[d]	$Pd(PPh_3)_4$ (3)	*n*-Bu_4NBr	DMF	80	n.r.

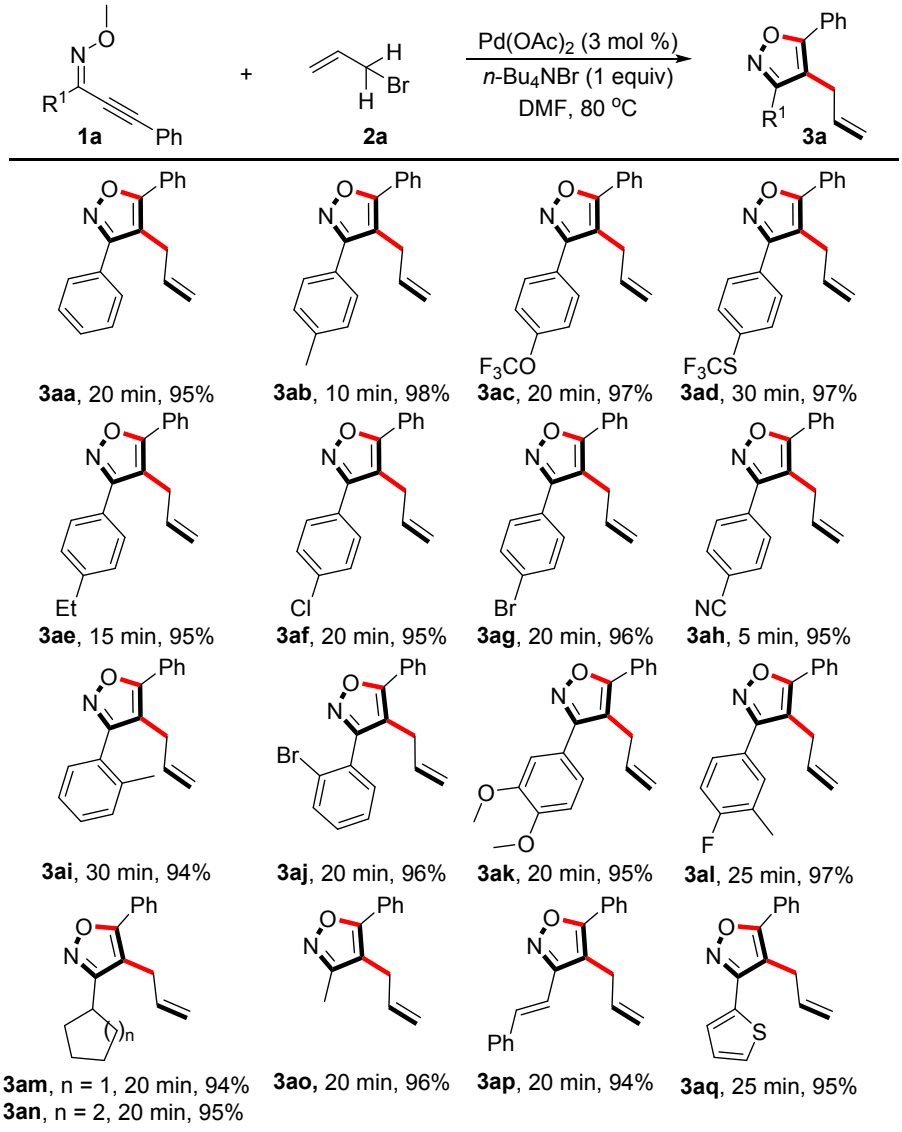
26[d]	$Pd(PCy_3)_2$ (3)	*n*-Bu_4NBr	DMF	80	n.r.
27[d]	$Pd_2(dba)_3$ (3)	*n*-Bu_4NBr	DMF	80	n.r.

[a]Reaction conditions: **1aa** (0.5 mmol), **2a** (0.6 mmol), [Pd] catalyst, additive (1.0 equiv), solvent (1.0 mL) were stirred for 3 h. [b]Detected by GC-MS using *n*-dodecane as internal standard. Data in the parentheses were referred to isolated yield. n.r. = no reaction. [c]The reaction time was 20 min. [d]Under N_2 atmosphere.

With the optimized conditions in hand, we first explored the substrate scope of alkynyl oxime ethers with different R^1 groups (Table 2). Generally, the substrates bearing different groups at the *ortho*-, *meta*- or *para*-position of the phenyl ring worked well and transformed to the isoxazole products in 95-98% yields in 10-30 min (**3aa**-**3aj**). For instance, functional groups such as -OCF_3 and -SCF_3 could be compatible under the standard reaction conditions, and the corresponding products **3ac** and **3ad** were assembled in excellent yields. It should be noted that the good tolerance with Cl and Br groups, which are known to undergo diverse Pd-mediated transformations, offered easy handles for further modification (**3af**, **3ag** and **3aj**). Moreover, the electron-donating groups could be also tolerated in this catalytic system, and the desired product **3ah** was formed in 95% yield in only 5 min. Multiple substituted aromatic substrates were found to be suitable for this catalytic system, converting to the corresponding products **3ak** and **3al** in excellent yields. In addition, the substrates with aliphatic substituents also proved to be effective in this allylation process and the target products could be obtained in 94-96% yields (**3am**-**3ao**).

Additionally, the reactions of styryl- and 2-thienyl- substituted alkynyl oxime ethers proceeded smoothly, leading to the allylation products **3ap** and **3aq** in 94% and 95% yields, respectively.

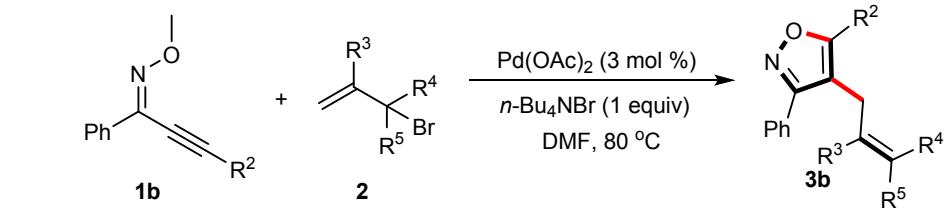
Table 2. Scope of Oxime Ethers with Different R^1 Groups[a]



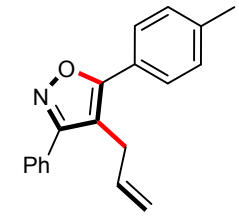
[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol, 1.2 equiv), $Pd(OAc)_2$ (3 mol %), *n*-Bu_4NBr (1.0 equiv), DMF (1.0 mL) were stirred at 80 °C for the indicated time. Yields referred to isolated yields.

The substrate scope of alkynyl oxime ethers bearing different R^2 groups and different terminal alkenes was then investigated. As shown in Table 3, substrates containing functional groups, such as Me, OEt, Ph, pentyloxy, F, Br at the *ortho*-, *meta*- or *para*-position exhibited good to excellent tolerance to this transformation (**3ba-3bm**). When R^2 = Ar, different length of aliphatic substituents at the phenyl ring were allowed to react with allyl bromide (**2a**), giving the corresponding products in good to excellent yields (**3bg-3bj**). Notably, the thienyl alkynyl oxime ether was also a suitable substrate, converting to the desired product **3bn** in 95% yield. In addition, the transformations of substrates with cyclopentyl and cyclohexyl moiety could also occur to afford the allylated products in 95% (**3bo**) and 93% yields (**3bp**), respectively. Gratifyingly, the linear chain aliphatic substrates were good candidates to deliver the target products in good yields (**3bq-3bt**). When the branched chain olefins were used, the corresponding products **3bu** and **3bv** could be generated in 97% and 95% yields, respectively. However, when disubstituted allyl bromide or trisubstituted allyl bromide were used as the allyl sources, the desired products could not be detected (**3bw** and **3bx**).

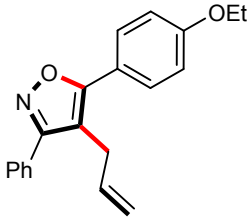
Table 3. Scope of Oxime Ethers with Different R^2 Groups and Alkenes[a]



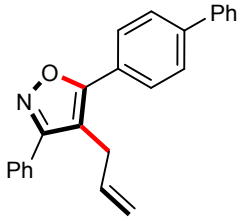
1b **2** **3b**



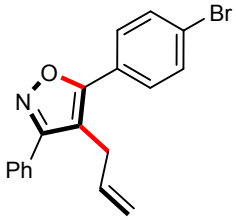
3ba, 10 min, 98%



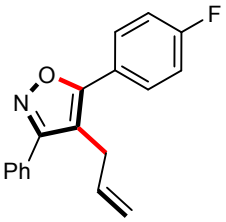
3bb, 25 min, 98%



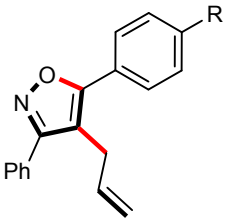
3bc, 40 min, 95%



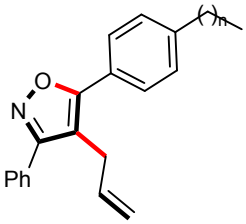
3bd, 40 min, 95%



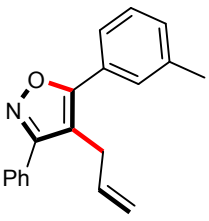
3be, 15 min, 97%



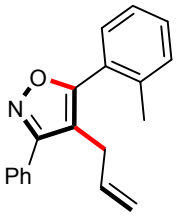
3bf, R = pentyloxy, 15 min, 98%



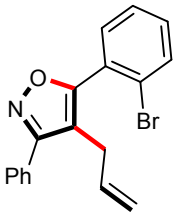
3bg, n = 1, 15 min, 97%
3bh, n = 2, 15 min, 97%
3bi, n = 3, 20 min, 96%
3bj, n = 4, 20 min, 94%



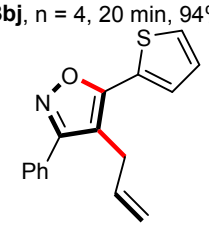
3bk, 15 min, 95%



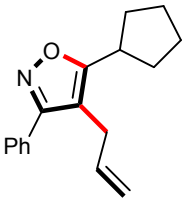
3bl, 30 min, 94%



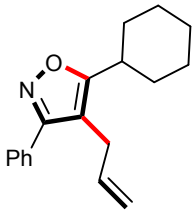
3bm, 35 min, 94%



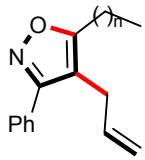
3bn, 35 min, 95%



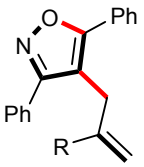
3bo, 20 min, 95%



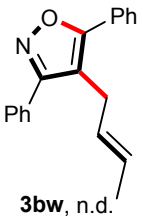
3bp, 20 min, 93%



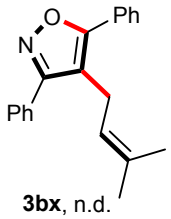
3bq, n = 2, 25 min, 93%
3br, n = 3, 20 min, 97%
3bs, n = 4, 20 min, 95%
3bt, 5 = 5, 30 min, 94%



3bu, R = Me, 30 min, 97%;
3bv, R = Br, 30 min, 95%;



3bw, n.d.

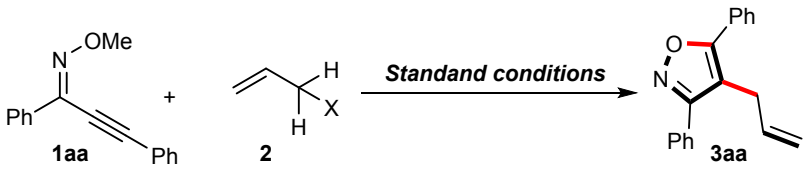


3bx, n.d.

[a]Reaction conditions: **1b** (0.5 mmol), **2** (0.6 mmol, 1.2 equiv), $Pd(OAc)_2$ (3 mol %), *n*-Bu_4NBr (1.0 equiv), DMF (1.0 mL) were stirred at 80 °C for the indicated time. Yields referred to isolated yields. n.d. = not detected.

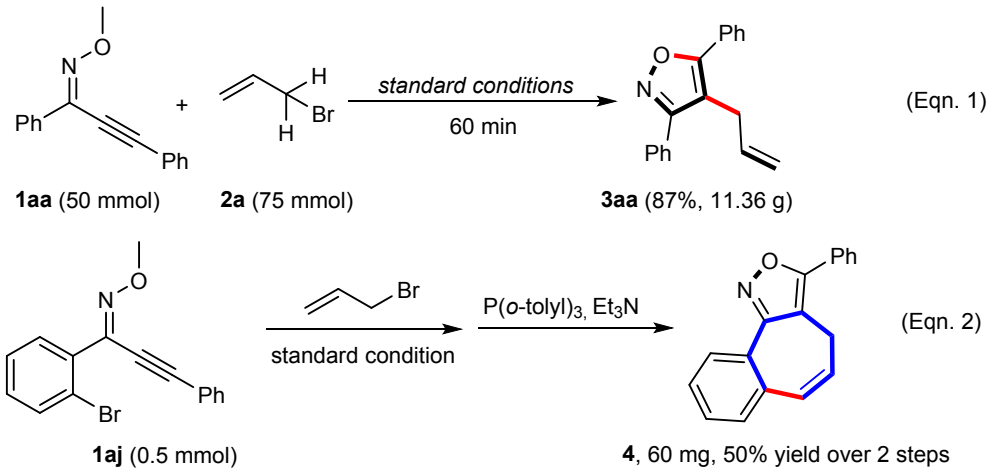
Additionally, other allyl halide compounds such as allyl chloride and allyl iodide could also be applied to this chemical process, and the desired product **3aa** was given respectively in 70% and 60% yields (Table 4), thus broadening the substrate scope of this synthetic method. However, no desired product was detected when propenol or allyl acetate was used as the substrate.

Table 4. Evaluation of Different Substituent of Alkenes



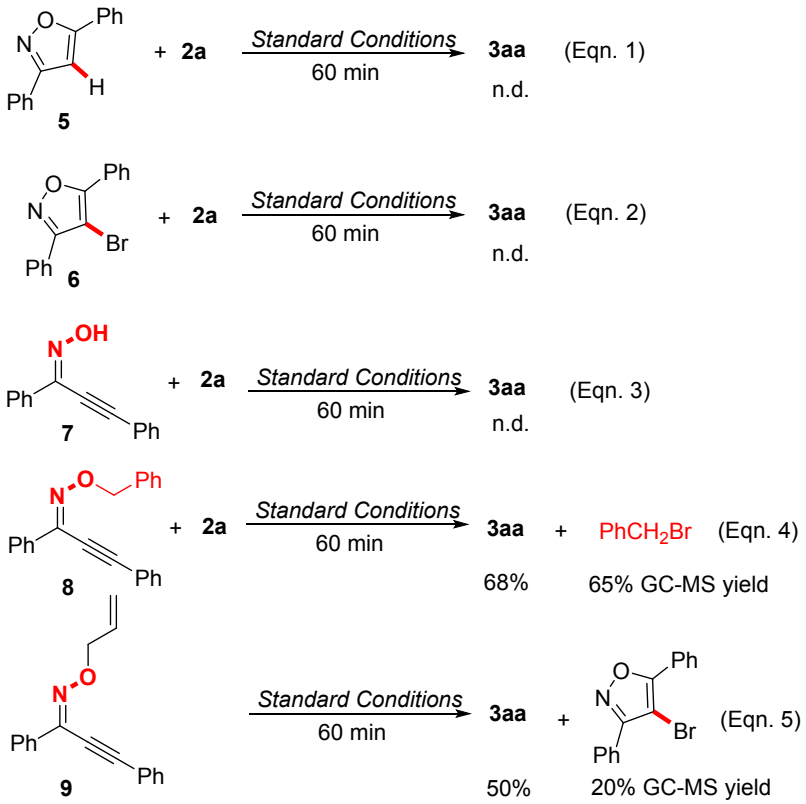
entry	X	reaction time/min	yield of **3aa** (%)
1	Cl	40	70
2	Br	20	95
3	I	30	60
4	OH	60	n.d.
5	OAc	60	n.d.

A 10-gram scale synthesis was then performed (Scheme 2, Eqn. 1), which further demonstrated the utility of this method. When 50 mmol of alkynyl oxime ether (**1aa**) was reacted with 75 mmol of allyl bromide (**2a**) under the standard reaction conditions, 11.36 g of **3aa** was isolated in 60 min. To demonstrate the synthetic utility of this protocol, the newly formed allylated products were employed for further elaborations. For example, the fused seven-membered ring compound **4** could be obtained in 50% yield over 2 steps from the starting material **1aj** (Scheme 2, Eqn. 2).[23]



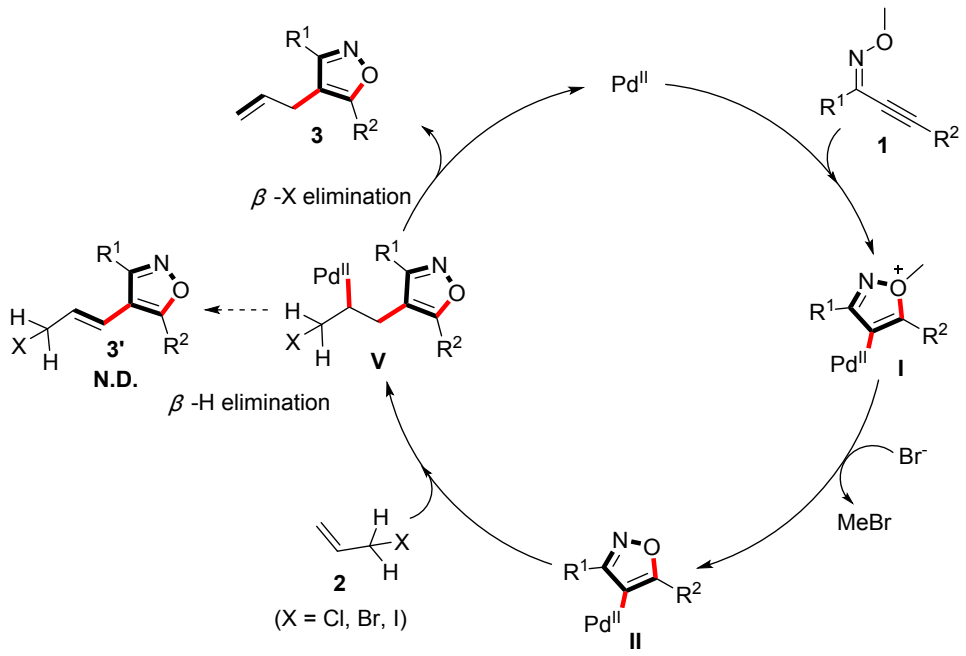
Scheme 2. Scale-up Experiment and Late-stage Transformations of the Newly Formed Products

Several control experiments were performed to unravel this reaction mechanism (Scheme 3). Firstly, treatment of **5** and **2a** with 3 mol % of $Pd(OAc)_2$ and 1.0 equiv of *n*-Bu_4NBr could not give **3aa**, indicating that C-H activation was not involved in this transformation (Scheme 3, Eqn. 1). When using 4-bromoisoxazole (**6**) as the substrate, no desired product was detected under the standard conditions, which revealed that **6** should not be a possible intermediate in this process (Scheme 3, Eqn. 2). Moreover, no desired product **3aa** was detected when **7** was tested (Scheme 3, Eqn. 3). While **3aa** could be isolated in 68% yield under the standard conditions with **8** as the substrate, and benzyl bromide was detected by GC analysis in 65% yield (Scheme 3, Eqn. 4). Additionally, when using alkynyl oxime allyl ether **9** as the substrate without allyl bromide, the desired product **3aa** could be observed in 50% GC yield under the standard conditions, and 4-bromo-3,5-diphenylisoxazole **6** was detected in 20% GC yield (Scheme 3, Eqn. 5).



Scheme 3. Control Experiments

On the basis of the above results and previous reports, a plausible mechanism is described in Scheme 4. Firstly, heteroaryl palladium intermediate **I** was formed by Pd(II)-catalyzed *5-endo-dig* cyclization. Attacked by Nu^- (Br^-, Cl^- or I^-), intermediate **II** would be afforded after the loss of a methyl group.[17] Then, the intermediate **II** could undergo alkene insertion to afford intermediate **V**. Finally, the *β*-X (X = Cl, Br, I) elimination occurred to give the desired product **3**. It should be noted that product **3'** formed by *β*-H elimination of intermediate **V** could not be detected, indicating that *β*-heteroatom elimination was preferred in this process.



Scheme 4. Proposed Mechanism

CONCLUSION

In summary, we have developed an efficient palladium-catalyzed rapid cyclization reaction of alkynyl oxime ethers and 1-alkenyl halides. In this transformation, new C(sp^2)-O and C(sp^2)-C(sp^2) bonds are formed simultaneously with the high yield of a series of structurally diverse fullysubstituted isoxazoles in 5-45 min. Easy operation, good substrate scope, mild conditions, and convenient late-stage transformations of the products are other features of this reaction, thus providing a concise and practical strategy for 4-allylisoxazole derivatives and showing potential applications in the fields of biochemistry and medicinal chemistry.

EXPERIMENTAL SECTION

All purchased reagents and solvents were used without further purification unless otherwise noted. Analytical thin layer chromatography was performed by using

commercially prepared 100-400 mesh silica gel plates (GF_{254}) and visualization was effected at 254 nm. All the haloalkynes were prepared according to known procedures. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker DRX-400 spectrometer using $CDCl_3$ as solvent. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. Mass spectra were recorded on a Thermo Scientific ISQ gas chromatograph-mass spectrometer. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Bruker TENSOR 27 spectrometer. Melting points were determined with a Büchi Melting Point B-545 instrument.

General Procedure for the Preparation of Ynone *O*-Methyl Oximes

Typical Procedure I:

Step 1: $PdCl_2(PPh_3)_2$ (0.02 mmol, 0.4 mol %, 14 mg), CuI (0.1 mmol, 2 mol %, 19 mg), and triethylamine (10 mL) were added to a 50 mL round-bottom flask. The flask was flushed with nitrogen for 3 min, and the terminal acetylene (5.0 mmol) was added to the stirred suspension, followed by immediate dropwise addition of acyl chloride (6.5 mmol). The mixture was stirred at room temperature overnight. After the fully consumption of starting material by TCL detection. The resulting solution was extracted with diethyl ether (3 × 20 mL). The organic layers were combined and dried over anhydrous $MgSO_4$. The solvent was removed under a vacuum, and the residue was purified by flash column chromatography on silica gel using PE/EA as the eluent

to afford alkynone.

Step 2: Alkynone (3.5 mmol), methoxylamine hydrochloride (7.0 mmol, 2.0 equiv, 581 mg), anhydrous Na_2SO_4 (7.0 mmol, 2.0 equiv, 994 mg), pyridine (1 mL), methanol (10 mL) were added to a 50 mL round-bottom flask. The reaction mixture was stirred at room temperature overnight. The mixture was diluted with saturated NH_4Cl solution (25 mL) and extracted with EtOAc (3 × 25 mL). The organic layers were combined, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed under a vacuum, and the residue was purified by flash column chromatography on silica gel using PE/EA as the eluent.

1ab, **1ac**, **1af-1aj**, **1al**, **1an**, **1ao**, **1ba**, **1be**, **1bj**, **1bn**, **1br**, **1bt** are known compounds and the NMR data are in good agreement with the literature[17-20]. **1aa**, **1ad**, **1ae**, **1ak**, **1am**, **1ap**, **1aq**, **1bb-1bd**, **1bf-1bi**, **1bk-1bm**, **1bo-1bq and 1bs** are unknown compounds and the corresponding NMR spectra data are shown as bellow:

(*Z*)-1,3-Diphenylprop-2-yn-1-one *O*-Methyl Oxime (1aa): R_f = 0.60 (PE/EA = 150: 1); 200 mg, 85% yield, white solid, mp: 98 - 99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19-7.74 (m, 2H), 7.59 (d, J = 3.0 Hz, 2H), 7.35 (d, J = 11.4 Hz, 6H), 4.12 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 140.0, 133.7, 132.3, 129.8, 129.7, 128.6, 126.6, 121.9, 101.3, 79.6, 63.2; IR (KBr)ν_{max}/cm^{-1}: 3065, 2933, 2206, 1453, 1332, 1046, 912, 761, 672, 530; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{16}H_{14}NO$, 236.1070, found: 236.1069.

(*Z*)-3-Phenyl-1-(4-((trifluoromethyl)thio)phenyl)prop-2-yn-1-one *O*-Methyl

Oxime (1ad): R_f = 0.50 (PE/EA = 150: 1); 275 mg, 82% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.6 Hz, 2H), 7.66 (d, J = 7.8 Hz, 2H), 7.60 (d, J = 7.6 Hz, 2H), 7.42-7.31 (m, 3H), 4.14 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 138.8, 136.1 (d, $J_{C\text{-}F}$ = 4.1 Hz), 132.2, 129.8, 128.0 (q, $J_{C\text{-}F}$ = 257.9 Hz), 127.2, 125.7 (q, $J_{C\text{-}F}$ = 1.7 Hz), 121.5, 101.9, 78.9, 63.4 (d, $J_{C\text{-}F}$ = 2.8 Hz); IR (KBr)ν_{max}/cm^{-1}: 2940, 2821, 2207, 1581, 1333, 1134, 1056, 916, 837, 758, 688, 512; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{17}H_{13}F_3NOS$, 336.0670, found, 336.0671.

(*Z*)-1-(4-Ethylphenyl)-3-phenylprop-2-yn-1-one *O*-methyl Oxime (1ae): R_f = 0.45 (PE/EA = 150: 1); 200 mg, 76% yield, yellow solid, mp: 104 - 105 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.0 Hz, 2H), 7.55- 7.48 (m, 2H), 7.28 (d, J = 5.6 Hz, 3H), 7.13 (d, J = 8.0 Hz, 2H), 4.03 (s, 3H), 2.58 (q, J = 7.6 Hz, 2H), 1.15 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 146.2, 140.0, 132.2, 131.2, 130.0, 128.5, 128.0, 126.6, 121.9, 100.9, 79.7, 63.1, 28.8, 15.5; IR (KBr)ν_{max}/cm^{-1}: 2972, 2207, 1760, 1247, 1044, 525; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{18}NO$, 264.1383, found: 264.1379.

(*Z*)-1-(3,4-Dimethoxyphenyl)-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1ak): R_f = 0.50 (PE/EA = 200: 1); 266 mg, 90% yield, white solid, mp: 111 - 112 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 7.4 Hz, 2H), 7.49 (d, J = 7.6 Hz, 2H), 7.37 (d, J = 6.0 Hz, 3H), 6.88 (d, J = 8.4 Hz, 1H), 4.12 (s, 3H), 3.94 (s, 3H), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 150.6, 148.9, 139.6, 132.1, 129.5, 128.5, 126.5, 121.9, 120.4, 110.7, 108.5, 100.8, 63.0, 62.9, 55.9; IR (KBr)ν_{max}/cm^{-1}: 2949, 2206, 1762, 1248, 1043, 761, 515; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{18}NO_3$, 296.1281,

found: 296.1286.

(*Z*)-1-Cyclopentyl-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1am): R_f = 0.50 (PE/EA = 200: 1); 197 mg, 87% yield, black oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (t, J = 6.7 Hz, 2H), 7.34 (d, J = 6.0 Hz, 3H), 3.96 (s, 3H), 2.05-1.50 (m, 10H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.8, 132.1, 131.9, 129.3, 128.4, 99.8, 79.4, 43.9, 31.1, 30.6, 25.8; IR (KBr)ν_{max}/cm^{-1}: 3067, 2209, 1760, 1475, 1340, 1242, 1047, 526; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{15}H_{18}NO$, 228.1383, found: 228.1381.

***(1E,3Z)*-1,5-Diphenylpent-1-en-4-yn-3-one *O*-Methyl Oxime (1ap)**: R_f = 0.60 (PE/EA = 150: 1); 224 mg, 86% yield, black solid, mp: 98 - 99 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (s, 2H), 7.42 (d, J = 21.7 Hz, 2H), 7.32- 7.11 (m, 7H), 6.83 (d, J = 15.9 Hz, 1H), 3.98 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 141.5, 139.4, 136.3, 136.1, 132.2, 132.1, 129.6, 129.5, 129.2, 128.8, 128.7, 128.5, 127.9, 127.2, 123.4, 121.7, 116.3, 101.0, 77.9, 63.1; IR (KBr)ν_{max}/cm^{-1}: 3065, 2928, 2208, 1763, 1452, 1048, 909, 754, 440; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{16}NO$, 262.1226, found: 262.1227.

***(E)*-3-Phenyl-1-(thiophen-2-yl)prop-2-yn-1-one *O*-Methyl Oxime (1aq)**: R_f = 0.45 (PE/EA = 200: 1); 193 mg, 80% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, J = 6.2, 2.6 Hz, 2H), 7.64 (d, J = 2.8 Hz, 1H), 7.39-7.34 (m, 3H), 7.31-7.21 (m, 2H), 4.11 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 139.9, 133.8, 130.9, 129.9, 129.7, 128.4, 126.6, 125.7, 121.0, 96.4, 79.4, 63.1; IR (KBr)ν_{max}/cm^{-1}: 3052, 2816, 2209, 1750, 1334, 1049, 911, 758, 524; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{14}H_{12}NOS$, 242.0634, found: 242.0631.

***(Z)*-3-(4-Ethoxyphenyl)-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bb)**: R_f = 0.50 (PE/EA = 150: 1); 237 mg, 85% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 5.0 Hz, 2H), 7.53 (d, J = 7.8 Hz, 2H), 7.38 (d, J = 4.8 Hz, 3H), 6.86 (d, J = 7.8 Hz, 2H), 4.12 (s, 3H), 4.02 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.1, 140.2, 133.9, 133.8, 129.6, 128.4, 126.6, 114.6, 113.6, 101.8, 78.6, 63.6, 63.1, 14.7; IR (KBr)ν_{max}/cm^{-1}: 3057, 2662, 2207, 1703, 1455, 1046, 970, 523; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{18}NO_2$, 280.1332, found: 280.1335.

***(Z)*-3-([1,1'-Biphenyl]-4-yl)-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bc)**: R_f = 0.45 (PE/EA = 150: 1); 266 mg, 85% yield, white solid, mp: 98 - 99 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.77 (m, 2H), 7.55 (d, J = 7.6 Hz, 2H), 7.46 (d, J = 8.8 Hz, 4H), 7.35- 7.20 (m, 6H), 4.02 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 142.4, 140.1, 140.0, 133.7, 132.7, 129.8, 129.0, 128.6, 128.0, 127.2, 127.1, 126.6, 120.7, 101.3, 80.3, 63.2; IR (KBr)ν_{max}/cm^{-1}: 3066, 2208, 1579, 1453, 1321, 1159, 1047, 908, 754, 521; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{18}NO$, 312.1383, found: 312.1389.

***(Z)*-3-(4-Bromophenyl)-1-phenylprop-2-yn-1-one *O*-methyl oxime (1bd)**: R_f = 0.50 (PE/EA = 100: 1); 231 mg, 88% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 4.4 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.39 (s, 3H), 4.13 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 139.7, 133.6, 133.4, 131.8, 129.8, 128.5, 126.5, 124.1, 120.8, 99.9, 80.5, 63.2; IR (KBr)ν_{max}/cm^{-1}: 3054, 2944, 2203, 1527, 1334, 1047, 915, 825, 667, 541; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for

$C_{16}H_{13}BrNO$, 314.0175, found：314.0182.

***(Z)*-3-(4-(Pentyloxy)phenyl)-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bf)**: R_f = 0.30 (PE/EA = 150: 1); 236 mg, 85% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04-7.92 (m, 2H), 7.60 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 5.0 Hz, 3H), 6.93 (d, J = 8.6 Hz, 2H), 4.19 (s, 3H), 4.00 (t, J = 6.6 Hz, 2H), 1.92- 1.75 (m, 2H), 1.58-1.36 (m, 4H), 0.99 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.3, 140.2, 133.9, 129.6, 128.4, 126.6, 114.7, 113.6, 101.9, 78.7, 68.2, 63.1, 28.9, 28.2, 22.5, 14.1; IR (KBr)ν_{max}/cm^{-1}: 3047, 2935, 2462, 2204, 1334, 1046, 912, 817, 662, 516; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}NO_2$, 322.1797, found: 322.1802.

***(Z)*-3-(4-Ethylphenyl)-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bg)**: R_f = 0.30 (PE/EA = 150: 1); 221 mg, 76% yield, yellow solid, mp: 99 - 100 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (dd, J = 6.6, 3.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.46 (dd, J = 5.0, 1.8 Hz, 3H), 7.27 (d, J = 8.0 Hz, 2H), 4.21 (s, 3H), 2.73 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 146.2, 140.1, 133.8, 132.3, 129.7, 128.5, 128.1, 126.6, 119.1, 101.7, 79.1, 63.1, 28.9, 15.3; IR (KBr)ν_{max}/cm^{-1}: 3055, 2207, 1760, 1242, 1048, 913, 678; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{18}NO$, 264.1383, found：264.1381.

***(Z)*-1-Phenyl-3-(4-propylphenyl)prop-2-yn-1-one *O*-Methyl Oxime (1bh)**: R_f = 0.50 (PE/EA = 150: 1); 211 mg, 85% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02-7.81 (m, 2H), 7.51 (d, J = 7.4 Hz, 2H), 7.36 (d, J = 5.2 Hz, 3H), 7.14 (d, J = 7.6 Hz, 2H), 4.11 (s, 3H), 2.56 (t, J = 7.6 Hz, 2H), 1.94- 1.39 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.7, 140.1, 133.8, 132.2, 129.7,

128.7, 128.5, 126.6, 119.1, 101.7, 79.2, 63.1, 38.1, 24.4, 13.8; IR (KBr)ν_{max}/cm^{-1}: 3047, 2937, 2203, 1447, 1334, 1046, 915, 666; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{20}NO$, 278.1539, found: 278.1540.

***(Z)*-3-(4-Butylphenyl)-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bi)**: R_f = 0.50 (PE/EA = 100: 1); 222 mg, 89% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, J = 6.6, 3.0 Hz, 2H), 7.60 (d, J = 8.1 Hz, 2H), 7.50-7.37 (m, 3H), 7.25 (d, J = 8.0 Hz, 2H), 4.21 (s, 3H), 2.76-2.62 (m, 2H), 1.75-1.56 (m, 2H), 1.51-1.35 (m, 2H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.9, 140.1, 133.8, 132.2, 129.7, 128.6, 128.4, 126.6, 119.0, 101.7, 79.1, 63.1, 35.7, 33.4, 22.4, 13.9; IR (KBr)ν_{max}/cm^{-1}: 3066, 2946, 2204, 1960, 1335, 1046, 915, 544; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{22}NO$, 292.1691, found：292.1696.

***(Z)*-1-Phenyl-3-(*m*-tolyl)prop-2-yn-1-one *O*-Methyl Oxime (1bk)**: R_f = 0.45 (PE/EA = 150: 1); 272 mg, 87% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 4.2 Hz, 2H), 7.49 (d, J = 7.4 Hz, 2H), 7.37 (s, 3H), 7.15 (d, J = 7.4 Hz, 2H), 4.12 (s, 3H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.1, 133.8, 132.1, 129.7, 129.3, 128.5, 126.6, 118.8, 101.7, 79.1, 63.2, 21.7; IR (KBr)ν_{max}/cm^{-1}: 3070, 2211, 1761, 1477, 1242, 1047, 912; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{17}H_{16}NO$, 250.1226, found: 250.1223.

***(Z)*-1-Phenyl-3-(*o*-tolyl)prop-2-yn-1-one *O*-Methyl Oxime (1bl)**: R_f = 0.60 (PE/EA = 150: 1); 200 mg, 88% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J = 4.2 Hz, 2H), 7.49 (d, J = 7.4 Hz, 2H), 7.37 (s, 3H), 7.15 (d, J = 7.4 Hz, 2H), 4.12 (s, 3H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.7, 133.8, 132.1, 129.7,

129.4, 128.5, 126.6, 118.8, 101.6, 79.1, 63.2, 21.7; IR (KBr)ν_{max}/cm^{-1}: 2940, 2217, 1763, 1326, 1050, 886, 767; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{17}H_{16}NO$, 250.1226, found：250.1232.

***(Z)*-3-(2-Bromophenyl)-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bm)**: R_f = 0.50 (PE/EA = 100: 1); 178 mg, 74% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 4.4 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.39 (s, 3H), 4.13 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 139.7, 133.6, 133.4, 131.8, 129.8, 128.5, 126.5, 124.1, 120.8, 99.9, 80.5, 63.2; IR (KBr)ν_{max}/cm^{-1}: 2940, 2207, 1758, 1242, 1049; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{16}H_{13}BrNO$, 314.0175, found: 314.0171.

***(Z)*-3-Cyclopentyl-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bo)**: R_f = 0.50 (PE/EA = 100: 1); 159 mg, 79% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (t, J = 6.7 Hz, 2H), 7.34 (d, J = 6.0 Hz, 3H), 3.96 (s, 3H), 2.17-1.48 (m, 10H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.8, 132.1, 131.9, 129.3, 128.4, 99.8, 79.4, 62.3, 43.9, 31.1, 30.6, 25.8; IR (KBr)ν_{max}/cm^{-1}: 3066, 2946, 2204, 1967, 1335, 1046, 915, 523; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{15}H_{18}NO$, 228.1383, found: 228.1384.

***(Z)*-3-Cyclohexyl-1-phenylprop-2-yn-1-one *O*-Methyl Oxime (1bp)**: R_f = 0.50 (PE/EA = 200: 1); 167 mg, 78% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (s, 2H), 7.35 (d, J = 6.0 Hz, 3H), 3.96 (s, 3H), 2.41 (t, J = 11.7 Hz, 1H), 1.84 (dd, J = 30.2, 11.3 Hz, 4H), 1.70 (d, J = 12.1 Hz, 1H), 1.51 (dd, J = 25.5, 12.9 Hz, 2H), 1.41-1.14 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 146.4, 132.1, 131.9, 129.3,

128.4, 121.9, 100.2, 79.5, 62.2, 43.0, 36.9, 30.8, 29.5, 25.9, 25.8, 25.8; IR (KBr)ν_{max}/cm^{-1}: 2999, 2210, 1761, 1242, 1049, 522; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{16}H_{20}NO$, 242.1539, found: 242.1545.

***(Z)*-1-Phenylhex-2-yn-1-one *O*-Methyl Oxime (1bq)**: R_f = 0.50 (PE/EA = 150:1); 177 mg, 90% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10-7.72 (m, 2H), 7.52-7.22 (m, 3H), 4.07 (s, 3H), 2.50 (t, J = 7.0 Hz, 2H), 1.67 (h, J = 7.2 Hz, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.2, 133.9, 129.5, 128.3, 126.5, 103.8, 71.7, 62.9, 21.8, 13.6; IR (KBr)ν_{max}/cm^{-1}: 3052, 1859, 1643, 1242, 1048, 688; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{13}H_{16}NO$, 202.1226, found:202.1226.

***(Z)*-1-Phenyloct-2-yn-1-one *O*-Methyl Oxime (1bs)**: R_f = 0.60 (PE/EA = 80: 1); 200 mg, 86% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (ddd, J = 5.8, 3.0, 1.4 Hz, 2H), 7.47-7.28 (m, 3H), 4.08 (s, 3H), 2.53 (t, J = 7.2 Hz, 2H), 1.73-1.60 (m, 2H), 1.45 (ddd, J = 11.6, 8.2, 4.8 Hz, 2H), 1.36 (dd, J = 14.8, 7.2 Hz, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.3, 134.0, 129.5, 128.3, 126.5, 103.9, 71.6, 62.9, 31.1, 28.0, 22.2, 19.8, 13.9; IR (KBr)ν_{max}/cm^{-1}: 3062, 2941, 2217, 1451, 1326, 1052, 767, 686, 552; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{15}H_{20}NO$, 230.1539, found: 230.1540.

General Procedure for the Synthesis of Isoxazole Derivatives

Typical Procedure Ⅱ: $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), alkynes **1** (0.5 mmol), and alkenes **2** (0.6 mmol) were added into a test tube successively, and stirred at 80 ^{o}C (oil bath) under open air. Upon full

consumption of the starting materials detected by TLC, the reaction was quenched by saturated NH_4Cl (aq.) after cooling to room temperature and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography using PE/EA (100:1~50:1) as eluent to afford the desired products **3**.

4-Allyl-3,5-diphenylisoxazole (**3aa**)[23]: Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1aa** (117.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3aa**. R_f = 0.30 (PE/EA = 60: 1); 124 mg, 95% yield, white solid, mp: 100 - 101 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, J = 6.8 Hz, 2H), 7.70 (dd, J = 6.4, 3.0 Hz, 2H), 7.47 (dd, J = 6.4 Hz, 6H), 6.15 - 6.04 (m, 1H), 5.25 (d, J = 10.4 Hz, 1H), 5.09 (d, J = 17.2 Hz, 1H), 3.46 - 3.39 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 164.0, 135.4, 129.8, 129.6, 129.4, 128.9, 128.7, 128.4, 128.2, 126.9, 117.1, 110.1, 27.1; IR (KBr)ν_{max}/cm^{-1}: 3066, 2916, 2845, 1963, 1891, 1815, 1624, 1422, 1261, 1167, 1071, 922, 838, 757, 694, 583, 484; MS (EI) m/z 77, 105, 129, 156, 261; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{16}NO$, 262.1226, found 262.1229.

4-Allyl-5-phenyl-3-(*p*-tolyl)isoxazole (3ab): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ab** (125.4 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ab**. R_f = 0.45 (PE/EA = 60: 1); 135 mg, 98% yield, white solid, mp: 102 -103 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 - 7.72 (m, 2H), 7.59 (d, J = 8.0 Hz, 2H), 7.44 (tdd, J = 6.8, 4.6, 2.4 Hz, 3H), 7.25 (d, J = 8.0 Hz, 2H), 6.15 - 6.01 (m, 1H), 5.22 (dd, J = 10.2, 1.4 Hz,

1H), 5.07 (dd, J = 17.4, 1.2 Hz, 1H), 3.40 (dd, J = 4.4, 2.1 Hz, 2H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):δ 166.7, 164.0, 139.6, 135.5, 129.8, 129.5, 128.9, 128.3, 126.9, 126.6, 117.1, 110.2, 27.2, 21.4; IR (KBr)ν_{max}/cm^{-1}: 3068, 2918, 1623, 1497, 1430, 1335, 1117, 1073, 1031, 919, 824, 759, 694, 578, 497; MS (EI) m/z 77, 105, 155, 170, 275; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO$, 276.1383, found 276.1381.

4-Allyl-5-phenyl-3-(4-(trifluoromethoxy)phenyl)isoxazole (3ac): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ac** (159.6 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ac**. R_f = 0.30 (PE/EA = 100: 1); 130 mg, 97% yield, white solid, mp: 103-104 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J = 9.0, 2.0 Hz, 4H), 7.47 (dt, J = 15.0, 5.0 Hz, 3H), 7.31 (d, J = 8.3 Hz, 2H), 6.15 - 6.03 (m, 1H), 5.26 (dd, J = 10.2, 1.0 Hz, 1H), 5.07 (dd, J = 17.4, 1.0 Hz, 1H), 3.44 - 3.35 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.3, 162.9, 150.2 (q, $J_{C\text{-}F}$ = 1.7 Hz), 135.2, 130.0, 128.9, 128.1, 127.9, 126.9, 121.1, 120.5 (q, $J_{C\text{-}F}$ = 257.9 Hz), 117.3, 109.9, 27.0; IR (KBr)ν_{max}/cm^{-1}: 3074, 2982, 2913, 1907, 1622, 1519, 1438, 1162, 1069, 1015, 922, 851, 761, 696, 585, 513, 440; MS (EI) m/z 77, 105, 155, 240, 345; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{15}F_3NO_2$, 346.1049, found 346.1046.

4-Allyl-5-phenyl-3-(4-((trifluoromethyl)thio)phenyl)isoxazole (3ad): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ad** (167.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ad**. R_f = 0.50 (PE/EA = 60: 1); 175 mg, 97% yield, white solid, mp:

105-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 - 7.74 (m, 6H), 7.51 (d, J = 7.0 Hz, 3H), 6.23 - 6.08 (m, 1H), 5.31 (d, J = 10.2 Hz, 1H), 5.12 (d, J = 17.3 Hz, 1H), 3.46 (d, J = 1.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.5, 162.8, 136.4, 135.2, 132.1, 130.1, 129.3, 129.0, 128.0 (q, $J_{C\text{-}F}$ = 255.3 Hz), 126.9, 126.0 (q, $J_{C\text{-}F}$ = 1.9 Hz), 125.9, 117.4, 110.0, 27.0; IR (KBr)$_{\nu max}$/cm^{-1}: 3072, 2914, 1634, 1430, 1296, 1122, 1014, 956, 920, 840, 758, 694, 584, 509; MS (EI) m/z 77, 105, 155, 256, 361; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{15}F_3NOS$, 362.0821, found 362.0826.

4-Allyl-3-(4-ethylphenyl)-5-phenylisoxazole (3ae): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ae** (131.6 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ae**. R_f = 0.30 (PE/EA = 80: 1); 137 mg, 95% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 7.4 Hz, 2H), 7.55 - 7.46 (m, 3H), 7.34 (d, J = 7.5 Hz, 2H), 6.22 - 6.07 (m, 1H), 5.29 (d, J = 10.2 Hz, 1H), 5.13 (d, J = 17.3 Hz, 1H), 3.47 (s, 2H), 2.75 (q, J = 7.4 Hz, 1H), 1.39 - 1.18 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.7, 164.0, 145.9, 135.5, 129.7, 128.9, 128.3, 128.3, 126.9, 126.7, 117.1, 110.1, 28.8, 27.2, 15.4; IR (KBr)ν_{max}/cm^{-1}: 3066, 2966, 2925, 2855, 1621, 1567, 1497, 1432, 1394, 1268, 1177, 1068, 996, 958, 919, 838, 758, 695, 581, 518; MS (EI) m/z 77, 105, 155, 184, 289; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{20}NO$, 290.1539, found 290.1538.

4-Allyl-3-(4-chlorophenyl)-5-phenylisoxazole (3af): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1af** (134.6 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3af**. R_f

= 0.60 (PE/EA = 100: 1); 140 mg, 95% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J = 134, 6.8 Hz, 3H), 7.59 (d, J = 7.3 Hz, 1H), 7.54 - 7.33 (m, 5H), 6.19 - 6.00 (m, 1H), 5.27 (d, J = 10.3 Hz, 1H), 5.08 (d, J = 17.3 Hz, 1H), 3.50 - 3.32 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.2, 162.8, 135.1, 134.7, 131.1, 130.0, 128.9, 128.4, 127.9, 126.9, 126.4, 117.3, 110.0, 27.0; IR (KBr)ν_{max}/cm^{-1}: 3073, 2915, 2817, 1566, 1496, 1442, 1387, 1267, 1171, 1080, 964, 918, 756, 692; MS (EI) m/z 77, 105, 155, 190, 295; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}ClNO$, 296.0837, found 296.0832.

4-Allyl-3-(4-bromophenyl)-5-phenylisoxazole (3ag): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ag** (156.6 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ag**. R_f = 0.30 (PE/EA = 30: 1). 163 mg, 96% yield, white solid, mp: 107-108 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 - 7.68 (m, 2H), 7.64 - 7.54 (m, 4H), 7.53 - 7.42 (m, 3H), 6.14 - 6.03 (m, 1H), 5.26 (dd, J = 10.2, 0.9 Hz, 1H), 5.07 (dd, J = 17.4, 0.9 Hz, 1H), 3.44 - 3.34 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.2, 163.1, 135.2, 132.0, 130.0, 129.9, 128.9, 128.3, 127.9, 126.9, 124.1, 117.3, 109.9, 27.0; IR (KBr)ν_{max}/cm^{-1}: 3066, 2918, 1598, 1496, 1427, 1384, 1267, 1171, 1073, 1009, 955, 920, 831, 757, 693, 583, 495; MS (EI) m/z 77, 105, 155, 234, 339; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNO$, 340.0332, found 340.0330.

4-(4-Allyl-5-phenylisoxazol-3-yl)benzonitrile (3ah): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ah** (130.1 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ah**. R_f

= 0.45 (PE/EA = 80: 1); 136 mg, 95% yield, white solid, mp: 100-101 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 - 7.82 (m, 2H), 7.81 - 7.72 (m, 4H), 7.55 - 7.45 (m, 3H), 6.16 - 6.05 (m, 1H), 5.29 (dd, J = 10.4, 1.2 Hz, 1H), 5.08 (dd, J = 17.2, 1.1 Hz, 1H), 3.43 (dt, J = 4.2, 2.0 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.8, 162.4, 135.0, 134.0, 132.5, 130.2, 129.0, 128.9, 127.7, 127.0, 118.4, 117.6, 113.4, 109.9, 26.9; MS (EI) m/z 77, 105, 271, 286; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{15}N_2O$, 287.1179, found, 287.1177.

4-Allyl-5-phenyl-3-(*o*-tolyl)isoxazole (3ai): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ai** (124.6 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ai**. R_f = 0.30 (PE/EA = 100: 1). 130 mg, 94% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.6 Hz, 2H), 7.48 (dd, J = 16.6, 9.0 Hz, 3H), 7.37 - 7.24 (m, 4H), 5.87 - 5.74 (m, 1H), 5.04 (d, J = 10.2 Hz, 1H), 4.92 (d, J = 17.2 Hz, 1H), 3.30 - 3.18 (m, 2H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.8, 164.6, 137.5, 134.6, 130.4, 129.8, 129.7, 129.4, 128.9, 128.7, 128.3, 126.8, 125.6, 116.4, 111.5, 26.9, 20.0; IR (KBr)ν_{max}/cm^{-1}: 3064, 2921, 1634, 1496, 1409, 1268, 1169, 1034, 994, 956, 915, 757, 694, 586; MS (EI) m/z 77, 105, 155, 184, 275; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO$, 276.1383, found 276.1381.

4-Allyl-3-(2-bromophenyl)-5-phenylisoxazole (3aj): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1aj** (156.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3aj**. R_f = 0.50 (PE/EA = 100: 1). 163 mg, 96% yield, white solid; mp: 100 - 101 ^{o}C; ^{1}H NMR

(400 MHz, $CDCl_3$): δ 7.82 - 7.76 (m, 2H), 7.68 (d, J = 7.7 Hz, 1H), 7.51 - 7.42 (m, 3H), 7.41 - 7.35 (m, 2H), 7.32 (ddd, J = 8.0, 5.9, 3.3 Hz, 1H), 5.82 - 5.68 (m, 1H), 5.03 - 4.84 (m, 2H), 3.30 (dt, J = 5.5, 1.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.0, 164.3, 134.4, 133.0, 131.7, 131.0, 130.8, 130.0, 129.0, 128.1, 127.3, 127.0, 123.5, 116.4, 114.2, 27.2; IR (KBr)ν_{max}/cm^{-1}: 3068, 2917, 1627, 1501, 1421, 1332, 1254, 1165, 1024, 917, 757, 690, 582; MS (EI) m/z 77, 105, 155, 236, 260, 339; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNO$, 340.0332, found, 340.0333.

4-Allyl-3-(3,4-dimethoxyphenyl)-5-phenylisoxazole (3ak): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ak** (147.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ak**. R_f = 0.30 (PE/EA = 80: 1); 152 mg, 95% yield, white solid, mp: 110-111 ^oC; ^{1} H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 7.1 Hz, 2H), 7.55 - 7.38 (m, 3H), 7.29 (d, J = 7.3 Hz, 2H), 6.95 (d, J = 8.5 Hz, 1H), 6.15 (ddd, J = 14.8, 9.7, 4.5 Hz, 1H), 5.29 (d, J = 10.3 Hz, 1H), 5.13 (d, J = 17.3 Hz, 1H), 3.91 (d, J = 1.4 Hz, 6H), 3.49 - 3.37 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.9, 163.7, 150.2, 149.1, 135.6, 129.8, 128.9, 128.2, 126.9, 122.0, 121.0, 117.2, 111.4, 111.2, 109.8, 56.0, 55.9, 27.2; IR (KBr)ν_{max}/cm^{-1}: 3074, 2937, 2836, 2584, 1599, 1521, 1439, 1329, 1528, 1147, 1025, 922, 863, 757, 696, 628, 518, 482; MS (EI) m/z 77, 105, 185, 216, 321; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{20}NO_3$, 322.1438, found 322.1439.

4-Allyl-3-(4-fluoro-3-methylphenyl)-5-phenylisoxazole (3al): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1al** (133.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol)

afforded **3al**. R_f = 0.30 (PE/EA = 50: 1); 142 mg, 97% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 - 7.71 (m, 2H), 7.56 (d, J = 7.1 Hz, 1H), 7.52 - 7.40 (m, 4H), 7.08 (t, J = 8.9 Hz, 1H), 6.16 - 6.03 (m, 1H), 5.26 (d, J = 10.5 Hz, 1H), 5.08 (d, J = 17.2 Hz, 1H), 3.48 - 3.33 (m, 2H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.9, 163.4, 162.2 (d, $J_{C\text{-}F}$ = 248.1 Hz).135.4, 131.7 (d, $J_{C\text{-}F}$ = 5.6 Hz), 129.9, 128.9, 128.1, 127.5 (d, $J_{C\text{-}F}$ = 8.4 Hz), 126.9, 125.5 (d, $J_{C\text{-}F}$ = 17.7 Hz), 125.2 (d, $J_{c\text{-}F}$ = 3.7 Hz), 117.2, 115.4 (d, $J_{C\text{-}F}$ = 22.8 Hz), 110.0, 27.1, 14.6 (d, $J_{C\text{-}F}$ = 3.2 Hz); IR (KBr)ν_{max}/cm^{-1}: 3070, 2921, 2851, 1891, 1603, 1508, 1434, 1325, 1250, 1182, 1119, 1057, 971, 970, 827, 755, 692, 615, 553, 441; MS (EI) m/z 77, 105, 173, 188, 293; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{17}FNO$, 294.1289, found 294.1292.

4-Allyl-3-cyclopentyl-5-phenylisoxazole (3am): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1am** (113.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3am**. R_f = 0.60 (PE/EA = 100: 1); 119 mg, 94% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, J = 8.1, 1.4 Hz, 2H), 7.48 - 7.34 (m, 3H), 5.99 (ddt, J = 17.1, 10.2, 5.1 Hz, 1H), 5.14 (dd, J = 10.2, 1.5 Hz, 1H), 5.02 (dd, J = 17.2, 1.5 Hz, 1H), 3.34 (dt, J = 4.9, 1.9 Hz, 2H), 3.03 (dd, J = 16.0, 8.0 Hz, 1H), 2.14 - 1.99 (m, 2H), 1.96 - 1.80 (m, 4H), 1.67 (dt, J = 8.2, 3.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.9, 165.6, 135.0, 129.5, 128.8, 128.5, 126.9, 116.4, 110.5, 36.4, 31.7, 26.7, 25.5; IR (KBr)ν_{max}/cm^{-1}: 3068, 2955, 2868, 1634, 1501, 1438, 1384, 1267, 1212, 1159, 1070, 985, 916, 757, 694; MS (EI) m/z 77, 105, 156, 212, 224, 253; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{17}H_{20}NO$, 254.1539, found 254.1540.

4-Allyl-3-cyclohexyl-5-phenylisoxazole (3an)[23]: Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1an** (120.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3an**. R_f = 0.40 (PE/EA = 80: 1); 127 mg, 95% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 - 7.56 (m, 2H), 7.56 - 7.34 (m, 3H), 6.01 (ddd, J = 22.2, 10.2, 5.1 Hz, 1H), 5.17 (dd, J = 10.2, 1.2 Hz, 1H), 5.04 (dd, J = 17.2, 1.2 Hz, 1H), 3.35 (dd, J = 3.1, 1.9 Hz, 2H), 2.71 - 2.57 (m, 1H), 2.00 (d, J = 12.6 Hz, 2H), 1.88 (d, J = 10.0 Hz, 2H), 1.79 - 1.61 (m, 3H), 1.35 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.4, 165.3, 135.2, 129.4, 128.8, 128.5, 126.9, 116.4, 109.9, 35.6, 31.8, 26.6, 26.5, 26.0; IR (KBr)ν_{max}/cm^{-1}: 3069, 2925, 2853, 1628, 1437, 1348, 1268, 1162, 1070, 980, 909, 830, 754, 690; MS (EI) m/z 77, 105, 162, 212, 248, 267; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{22}NO$, 268.1696, found 268.1697.

4-Allyl-3-methyl-5-phenylisoxazole (3ao): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ao** (86.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ao**. R_f = 0.45 (PE/EA = 100: 1); 96 mg, 96% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 7.8 Hz, 2H), 7.49 - 7.34 (m, 3H), 6.03 - 5.86 (m, 1H), 5.13 (d, J = 10.2 Hz, 1H), 5.01 (d, J = 17.1 Hz, 1H), 3.36 - 3.26 (m, 2H), 2.25 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.4, 161.0, 134.5, 129.6, 128.8, 128.4, 126.8, 116.3, 110.9, 26.8, 10.1; IR (KBr)ν_{max}/cm^{-1}: 3066, 2980, 2924, 2851, 1637, 1443, 1267, 1159, 1071, 999, 917, 756, 694, 637, 566, 444; MS (EI) m/z 77, 105, 129, 157, 184, 199; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{13}H_{14}NO$, 200.1070, found 200.1068.

(E)-4-Allyl-5-phenyl-3-styrylisoxazole (3ap): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ap** (130.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ap**. R_f = 0.40 (PE/EA = 80: 1); 135 mg, 94% yield, yellow solid, mp: 101-102 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 7.1 Hz, 2H), 7.55 - 7.42 (m, 6H), 7.37 (t, J = 7.1 Hz, 2H), 7.31 (d, J = 7.0 Hz, 1H), 6.94 (d, J = 16.5 Hz, 1H), 6.14 - 6.00 (m, 1H), 5.22 (d, J = 10.2 Hz, 1H), 5.10 (d, J = 17.2 Hz, 1H), 3.45 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5, 161.1, 136.3, 135.6, 134.8, 129.8, 128.9, 128.8, 128.1, 127.1, 127.0, 117.0, 114.7, 110.4, 27.0; IR (KBr)ν_{max}/cm^{-1}: 3057, 2918, 2849, 1961, 1888, 1817, 1629, 1499, 1431, 1272, 1197, 1072, 973, 917, 846, 756, 689, 564, 496; MS (EI) m/z 77, 105, 287; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{18}NO$, 288.1383, found 288.1379.

4-Allyl-5-phenyl-3-(thiophen-2-yl)isoxazole (3aq): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1aq** (120.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3aq**. R_f = 0.40 (PE/EA = 60: 1); 130 mg, 97% yield, white solid, mp: 101-102 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 6.8 Hz, 2H), 7.57 - 7.38 (m, 5H), 7.13 (d, J = 3.2 Hz, 1H), 6.21 - 6.05 (m, 1H), 5.25 (d, J = 10.2 Hz, 1H), 5.09 (d, J = 17.3 Hz, 1H), 3.50 (d, J = 2.0 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.4, 158.5, 134.8, 130.2, 130.0, 129.0, 127.9, 127.8, 127.7, 127.6, 127.0, 117.2, 109.8, 27.1; IR (KBr)ν_{max}/cm^{-1}: 3077, 2990, 2917, 2846, 1814, 1618, 1427, 1236, 1163, 1066, 994, 919, 842, 754, 575, 483; MS (EI) m/z 77, 105, 162, 238, 267; HRMS (ESI, m/z):

$[M+H]^+$ Calcd. for $C_{16}H_{14}NOS$, 268.0791, found 268.0795.

4-Allyl-3-phenyl-5-(*p*-tolyl)isoxazole (3ba): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1ba** (124.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3ba**. R_f = 0.30 (PE/EA = 80: 1); 135 mg, 98% yield, yellow solid, mp: 102-103 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 - 7.62 (m, 4H), 7.44 (d, J = 4.2 Hz, 3H), 7.25 (d, J = 7.8 Hz, 2H), 6.06 (ddd, J = 15.0, 9.8, 4.6 Hz, 1H), 5.21 (d, J = 10.8 Hz, 1H), 5.06 (d, J = 17.4 Hz, 1H), 3.52 - 3.28 (m, 2H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.1, 164.0, 140.0, 135.5, 129.7, 129.6, 129.6, 128.8, 128.4, 126.8, 125.4, 117.1, 109.6, 27.2, 21.5; IR (KBr)ν_{max}/cm^{-1}: 3069, 2997, 2915, 2844, 2417, 1903, 1620, 1516, 1431, 1333, 1270, 1179, 1117, 1021, 918, 830, 757, 694, 572, 495; MS (EI) m/z 77, 91, 119, 129, 156, 275; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO$, 276.1383, found 276.1382.

4-Allyl-5-(4-ethoxyphenyl)-3-phenylisoxazole (3bb): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bb** (1139.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bb**. R_f = 0.30 (PE/EA = 100: 1); 150 mg, 98% yield, white solid, mp: 110-111 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 - 7.66 (m, 4H), 7.54 - 7.44 (m, 3H), 7.02 (d, J = 8.8 Hz, 2H), 6.20 - 6.05 (m, 1H), 5.27 (dd, J = 10.2, 1.2 Hz, 1H), 5.12 (dd, J = 17.4, 1.2 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.50 - 3.36 (m, 2H), 1.47 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.0, 164.0, 160.2, 135.6, 129.6, 129.5, 128.7, 128.5, 128.4, 120.8, 117.0, 114.8, 108.8, 63.6, 27.2, 14.8; IR (KBr)ν_{max}/cm^{-1}: 3057,

2985, 2934, 2893, 1612, 1511, 1413, 1303, 1252, 1177, 1114, 1042, 918, 838, 744, 698, 639, 582, 518; MS (EI) m/z 77, 121, 149, 276, 305; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{20}NO_2$, 306.1489, found 306.1491.

5-([1,1'-Biphenyl]-4-yl)-4-allyl-3-phenylisoxazole (3bc): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bc** (155.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bc**. R_f = 0.40 (PE/EA = 100: 1); 160 mg, 95% yield, white solid, mp: 108-109 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 7.4 Hz, 4H), 7.63 (d, J = 7.6 Hz, 2H), 7.46 (t, J = 6.8 Hz, 5H), 7.38 (t, J = 7.2 Hz, 1H), 6.17 - 6.04 (m, 1H), 5.27 (d, J = 10.2 Hz, 1H), 5.11 (d, J = 17.2 Hz, 1H), 3.46 (d, J = 2.0 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.6, 164.2, 142.5, 140.2, 135.3, 129.6, 129.4, 129.0, 128.8, 128.4, 127.9, 127.6, 127.3, 127.1, 127.0, 117.2, 110.2, 27.2; IR (KBr)ν_{max}/cm^{-1}: 3063, 2921, 1618, 1488, 1447, 1409, 1266, 1171, 1001, 917, 842, 757, 695, 585, 495; MS (EI) m/z 77, 95, 184, 260, 337; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{20}NO$, 338.1539, found 338.1538.

4-Allyl-5-(4-bromophenyl)-3-phenylisoxazole (3bd): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bd** (156.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bd**. R_f = 0.30 (PE/EA = 60: 1); 161 mg, 95%, white solid, mp: 100-101 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 - 7.52 (m, 6H), 7.48 - 7.38 (m, 3H), 6.24 - 5.93 (m, 1H), 5.23 (dd, J = 10.4, 1.2 Hz, 1H), 5.04 (ddd, J = 17.2, 3.2, 1.8 Hz, 1H), 3.45 - 3.31 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.7, 164.2, 135.1, 132.2, 129.7, 129.2, 128.8,

128.4, 128.3, 127.0, 124.3, 117.3, 110.6, 27.1; IR (KBr)ν_{max}/cm^{-1}: 3071, 2914, 1615, 1425, 1271, 921, 747, 498; MS (EI) m/z 77, 129, 156, 183, 260, 339; HRMS (ESI, m/z): $[M+H]^+$ $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNO$, 340.0332, found, 340.0329.

4-Allyl-5-(4-fluorophenyl)-3-phenylisoxazole (3be): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1be** (1126.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3be**. R_f = 0.40 (PE/EA = 60: 1); 153 mg, 97% yield, white solid, mp: 107-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 - 7.73 (m, 2H), 7.72 - 7.65 (m, 2H), 7.52 - 7.45 (m, 3H), 7.18 (t, J = 8.6 Hz, 2H), 6.09 (ddd, J = 12.4, 10.2, 5.2 Hz, 1H), 5.26 (dd, J = 10.2, 1.1 Hz, 1H), 5.08 (dd, J = 17.4, 1.0 Hz, 1H), 3.43 - 3.33 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.0, 164.1, 163.5 (d, $J_{C\text{-}F}$ = 250.8 Hz), 135.2, 129.7, 129.3, 129.0 (d, $J_{C\text{-}F}$ = 8.5 Hz), 128.8, 128.4, 124.4 (d, $J_{C\text{-}F}$ = 3.4 Hz), 117.2, 116.1 (d, $J_{C\text{-}F}$ = 21.9 Hz), 109.9, 27.1; IR (KBr)ν_{max}/cm^{-1}: 3066, 2914, 1617, 1509, 1410, 1232, 1121, 1069, 1002, 928, 839, 756, 694, 573, 505; MS (EI) m/z 77, 95, 123, 129, 156, 250, 279; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}FNO$, 280.1132, found 280.1128.

4-Allyl-5-(4-(pentyloxy)phenyl)-3-phenylisoxazole (3bf): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bf** (160.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bf**. R_f = 0.60 (PE/EA = 100: 1); 170 mg, 98% yield, yellow solid, mp: 101-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 - 7.69 (m, 4H), 7.49 (dd, J = 5.0, 1.8 Hz, 3H), 7.03 (d, J = 8.8 Hz, 2H), 6.21 - 6.06 (m, 1H), 5.28 (dd, J = 10.2, 1.4 Hz, 1H), 5.12 (dd, J = 17.2, 1.4 Hz, 1H), 4.03 (t, J = 6.6 Hz, 2H), 3.60 - 3.34 (m, 2H), 1.90 -

1.74 (m, 2H), 1.58 - 1.40 (m, 4H), 0.98 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.0, 164.0, 160.4, 135.6, 129.6, 129.5, 128.7, 128.3, 120.6, 117.0, 114.9, 108.7, 68.2, 28.9, 28.2, 27.2, 22.5, 14.1; IR (KBr)ν_{max}/cm^{-1}: 3070, 2947, 2865, 1614, 1512, 1455, 1413, 1301, 1251, 1217, 1114, 1022, 957, 917, 835, 761, 698, 582, 519; MS (EI) m/z 77, 121, 156, 277, 347; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{26}NO_2$, 348.1958, found 348.1955.

4-Allyl-5-(4-ethylphenyl)-3-phenylisoxazole (3bg): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bg** (131.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bg**. R_f = 0.45 (PE/EA = 80: 1); 140 mg, 97% yield, white solid, mp: 110-111 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 7.0 Hz, 4H), 7.41 (s, 2H), 7.42 (s, 1H), 7.30 (d, J = 7.6 Hz, 2H), 6.21 - 5.93 (m, 1H), 5.23 (d, J = 10.2 Hz, 1H), 5.07 (d, J = 17.2 Hz, 1H), 3.40 (s, 2H), 2.69 (q, J = 7.4 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.1, 164.0, 146.3, 135.5, 129.6, 129.5, 128.7, 128.5, 128.4, 126.9, 125.7, 117.1, 109.6, 28.8, 27.1, 15.3; IR (KBr)ν_{max}/cm^{-1}: 2966, 2927, 1621, 1509, 1446, 1409, 1269, 1173, 959, 915, 836, 755, 696, 575, 517; MS (EI) m/z 77, 105, 129, 133, 156, 260, 289; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{20}NO$, 290.1539, found 290.1536.

4-Allyl-3-phenyl-5-(4-propylphenyl)isoxazole (3bh): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bh** (138.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bh**. R_f = 0.30 (PE/EA = 60: 1); 147 mg, 97% yield, white solid, mp: 112-113 ^{o}C; ^{1}H NMR

(400 MHz, $CDCl_3$): δ 7.69 (d, J = 7.0 Hz, 4H), 7.41 (s, 2H), 7.42 (s, 1H), 7.28 (d, J = 7.6 Hz, 2H), 6.17 - 6.02 (m, 1H), 5.23 (d, J = 10.2 Hz, 1H), 5.07 (d, J = 17.2 Hz, 1H), 3.41 (s, 2H), 2.63 (t, J = 7.4 Hz, 2H), 1.67 (dd, J = 14.8, 7.4 Hz, 2H), 0.96 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.1, 164.0, 144.7, 135.5, 129.6, 129.5, 129.0, 128.7, 128.4, 126.8, 125.7, 117.1, 109.6, 37.9, 27.1, 24.3, 13.8; IR (KBr)ν_{max}/cm^{-1}: 2960, 2926, 2863, 1619, 1509, 1447, 1409, 1269, 1173, 958, 916, 841, 756, 696, 579, 514; MS (EI) m/z 77, 91, 105, 147, 156, 260, 303; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{22}NO$, 304.1696, found 304.1692.

4-Allyl-5-(4-butylphenyl)-3-phenylisoxazole (3bi): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bi** (145.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bi**. R_f = 0.40 (PE/EA = 70: 1); 159 mg, 96% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 6.4 Hz, 4H), 7.46 (d, J = 2.2 Hz, 3H), 7.29 (d, J = 7.8 Hz, 2H), 6.17 - 6.01 (m, 1H), 5.24 (d, J = 10.2 Hz, 1H), 5.08 (d, J = 17.2 Hz, 1H), 3.41 (s, 2H), 2.66 (t, J = 7.4 Hz, 2H), 1.63 (dd, J = 15.0, 7.6 Hz, 2H), 1.38 (dd, J = 14.4, 7.2 Hz, 2H), 0.94 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.1, 164.0, 145.0, 135.5, 129.6, 129.5, 129.0, 128.7, 128.4, 126.8, 125.6, 117.0, 109.6, 35.6, 33.4, 27.1, 22.3, 13.9; IR (KBr)ν_{max}/cm^{-1}: 2966, 2927, 1625, 1509, 1448, 1383, 1267, 917, 838, 754, 698; MS (EI) m/z 77, 91, 129, 156, 161, 317; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{24}NO$, 318.1852, found 318.1850.

4-Allyl-5-(4-pentylphenyl)-3-phenylisoxazole (3bj): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), n-Bu_4NBr (1.0 equiv, 161 mg),

DMF (1.0 mL), **1bj** (152.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol)/toluene (1.0 mL) afforded **3bj**. R_f = 0.30 (PE/EA = 50: 1); 156 mg, 94% yield, yellow solid, mp: 111-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 - 7.65 (m, 4H), 7.44 (dd, J = 5.0, 1.8 Hz, 3H), 7.28 (d, J = 8.2 Hz, 2H), 6.08 (ddd, J = 12.6, 10.2, 5.2 Hz, 1H), 5.22 (dd, J = 10.2, 1.2 Hz, 1H), 5.07 (dd, J = 17.4, 1.2 Hz, 1H), 3.47 - 3.33 (m, 2H), 2.70 - 2.54 (m, 2H), 1.72 - 1.57 (m, 2H), 1.33 (dt, J = 7.4, 3.6 Hz, 4H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.1, 164.0, 145.0, 135.5, 129.6, 129.5, 129.0, 128.7, 128.4, 126.8, 125.6, 117.1, 109.6, 35.9, 31.5, 31.0, 27.2, 22.6, 14.1; IR (KBr)ν_{max}/cm^{-1}: 3067, 2927, 2858, 1621, 1510, 1449, 1441, 1269, 1177, 1119, 1074, 1024, 958, 918, 843, 757, 698, 581, 526; MS (EI) m/z 77, 91, 175, 260, 331; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{26}NO$, 332.2009, found 332.2008.

4-Allyl-3-phenyl-5-(*m*-tolyl)isoxazole (3bk): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bk** (124.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bk**. R_f = 0.30 (PE/EA = 80: 1); 131 mg, 95% yield, yellow solid, mp: 103-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (dd, J = 6.8, 2.8 Hz, 2H), 7.48 (s, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.36 - 7.29 (m, 3H), 7.22 (t, J = 7.8 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 6.02 - 5.87 (m, 1H), 5.11 (dd, J = 10.2, 1.2 Hz, 1H), 4.95 (dd, J = 17.2, 1.2 Hz, 1H), 3.32 - 3.23 (m, 2H), 2.28 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.1, 164.0, 138.7, 135.5, 130.7, 129.6, 129.5, 128.8, 128.7, 128.4, 128.1, 127.6, 124.1, 117.1, 110.1, 27.2, 21.5; IR (KBr)ν_{max}/cm^{-1}: 3064, 2975, 2918, 2854, 1590, 1447, 1409, 1249, 1169, 1088, 1031, 921, 843, 760, 701, 587, 438; MS (EI) m/z 77, 91, 119, 129, 156, 260, 275;

HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO$, 276.1383, found 276.1379.

4-Allyl-3-phenyl-5-(*o*-tolyl)isoxazole (3bl): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bl** (124.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bl**. R_f = 0.60 (PE/EA = 80: 1); 130 mg, 94% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 - 7.56 (m, 2H), 7.34 - 7.27 (m, 3H), 7.21 (t, J = 8.6 Hz, 2H), 7.15 (d, J = 7.2 Hz, 1H), 7.09 (t, J = 7.4 Hz, 1H), 5.68 (ddd, J = 15.6, 10.4, 5.2 Hz, 1H), 4.95 - 4.83 (m, 1H), 4.79 (dd, J = 17.2, 0.9 Hz, 1H), 3.17 - 3.06 (m, 2H), 2.21 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.5, 161.6, 137.0, 134.5, 129.7, 129.0, 128.6, 128.5 128.4, 127.6, 127.1, 126.5, 124.7, 115.4, 110.9, 25.7, 19.1; IR (KBr)ν_{max}/cm^{-1}: 3067, 2975, 2920, 2825, 1630, 1449, 1410, 1241, 1174, 1076, 1038, 995, 954, 918, 759, 698, 588, 450; MS (EI) m/z 77, 91, 119, 156, 260, 275; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO$, 276.1383, found 276.1384.

4-Allyl-5-(2-bromophenyl)-3-phenylisoxazole (3bm)[23]: Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bm** (156.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bm**. R_f = 0.50 (PE/EA = 80: 1); 159 mg, 94% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (dd, J = 12.6, 6.6 Hz, 3H), 7.49 - 7.31 (m, 6H), 5.83 - 5.70 (m, 1H), 4.95 (dd, J = 21.8, 13.6 Hz, 2H), 3.33 - 3.25 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.0, 162.8, 135.0, 133.4, 131.8, 131.7, 129.7, 129.6, 129.4, 128.8, 128.3, 127.4, 123.7, 116.6, 113.3, 27.0; IR (KBr)ν_{max}/cm^{-1}: 3067, 2918, 1634, 1575, 1442, 1408, 1254, 1068, 1026, 918, 757, 697, 584, 444; MS (EI) m/z 77, 129, 156,

183, 258, 339; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNO$, 340.0332, found 340.0336.

4-Allyl-3-phenyl-5-(thiophen-2-yl)isoxazole (3bn): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bn** (120.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bn**. R_f = 0.50 (PE/EA = 80: 1); 127 mg, 95% yield, black solid, mp: 107-108 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 1.8 Hz, 2H), 7.54 (m, 5H), 7.19 (s, 1H), 6.15 - 6.02 (m, 1H), 5.24 (d, J = 10.2 Hz, 1H), 5.11 (d, J = 17.2 Hz, 1H), 3.48 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.0, 162.4, 134.5, 129.7, 129.2, 128.8, 128.4, 127.9, 127.8, 127.1, 116.9, 109.7, 27.0; IR (KBr)ν_{max}/cm^{-1}: 3079, 2985, 2913, 2841, 1965,1816, 1617, 1522, 1437, 1339, 124, 1165, 1068, 1000, 925, 844, 754, 706, 577, 485; MS (EI) m/z 77, 111, 129, 156, 252, 267; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{16}H_{14}NOS$, 268.0791, found 268.0787.

4-Allyl-5-cyclopentyl-3-phenylisoxazole (3bo): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bo** (113.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bo**. R_f = 0.60 (PE/EA = 80: 1); 120 mg, 95% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 3.0 Hz, 2H), 7.41 (s, 2H), 7.42 (s, 1H), 6.06 - 5.86 (m, 1H), 5.11 (d, J = 10.0 Hz, 1H), 4.99 (d, J = 17.2 Hz, 1H), 3.32 - 3.16 (m, 3H), 2.04 (t, J = 11.4 Hz, 2H), 1.92 (s, 4H), 1.72 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.5, 162.8, 135.9, 129.9, 129.3, 128.6, 128.2, 116.0, 109.0, 36.7, 31.6, 26.3, 25.8; IR (KBr)ν_{max}/cm^{-1}: 3070, 2958, 2913, 2841, 1617, 1437, 1240, 1165, 1068, 1000, 925, 844, 754, 706, 577,

485; MS (EI) m/z 77, 156, 184, 238, 253; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{17}H_{20}NO$, 254.1539, found 254.1540.

4-Allyl-5-cyclohexyl-3-phenylisoxazole (3bp)[23]: Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bp** (120.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bp**. R_f = 0.60 (PE/EA = 80: 1); 124 mg, 93% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.65 - 7.56 (m, 2H), 7.42 (d, J = 1.8 Hz, 3H), 5.99 - 5.81 (m, 1H), 5.08 (d, J = 10.2 Hz, 1H), 4.96 (d, J = 17.2 Hz, 1H), 3.22 (d, J = 3.4 Hz, 2H), 2.77 (t, J = 11.8 Hz, 1H), 1.87 (d, J = 10.6 Hz, 4H), 1.71 (dd, J = 22.8, 11.4 Hz, 3H), 1.32 (dt, J = 25.6, 12.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.1, 162.7, 136.0, 129.9, 129.3, 128.6, 128.3, 116.0, 108.4, 36.2, 30.9, 26.2, 26.2, 25.7; IR (KBr)ν_{max}/cm^{-1}: 2928, 2852, 1618, 1446, 1269, 1271, 915, 755, 694; MS (EI) m/z 77, 156, 184, 252, 267; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{22}NO$, 268.1696, found 268.1695.

4-Allyl-3-phenyl-5-propylisoxazole (3bq): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bq** (100.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bq**. R_f = 0.35 (PE/EA = 80: 1); 106 mg, 93% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 - 7.61 (m, 2H), 7.50 - 7.41 (m, 3H), 5.91 (d, J = 7.6, 5.0 Hz, 1H), 5.09 (d, J = 10.0 Hz, 1H), 4.99 (d, J = 17.2 Hz, 1H), 3.24 (d, J = 3.4 Hz, 2H), 2.72 (t, J = 7.4 Hz, 2H), 1.78 (dd, J = 14.6, 7.4 Hz, 2H), 1.02 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.6, 162.6, 135.6, 129.9, 129.3, 128.6, 128.2, 116.0, 109.9, 27.6, 26.4, 21.0, 13.9; IR (KBr)ν_{max}/cm^{-1}: 3069, 2957, 1966, 1865, 1824, 1700, 1625, 1444, 1339, 1273,

1176, 1063, 992, 919, 761, 698, 564; MS (EI) m/z 77, 129, 212, 227; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{15}H_{18}NO$, 228.1383, found 228.1386.

4-Allyl-5-butyl-3-phenylisoxazole (3br)[23]: Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1br** (107.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3br**. R_f = 0.60 (PE/EA = 80: 1); 117 mg, 109 mg, 97% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, J = 6.4, 3.0 Hz, 2H), 7.48 - 7.40 (m, 3H), 5.88 (ddd, J = 15.6, 10.2, 5.2 Hz, 1H), 5.07 (dd, J = 10.2, 1.2 Hz, 1H), 4.96 (dd, J = 17.0, 1.4 Hz, 1H), 3.21 (d, J = 5.4 Hz, 2H), 2.71 (t, J = 7.6 Hz, 2H), 1.76 - 1.64 (m, 2H), 1.46 - 1.33 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.8, 162.7, 135.6, 129.8, 129.3, 128.6, 128.2, 116.0, 109.8, 29.7, 26.4, 25.4, 22.4, 13.7; IR (KBr)ν_{max}/cm^{-1}: 3069, 2932, 2836, 1624, 1452, 1288, 1172, 1062, 990, 913, 754, 698, 568; MS (EI) m/z 77, 129, 156, 184, 241; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{16}H_{20}NO$, 242.1539, found 242.1542.

4-Allyl-5-pentyl-3-phenylisoxazole (3bs): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bs** (114.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol)/toluene (1.0 mL) afforded **3bs**. R_f = 0.50 (PE/EA = 100: 1); 128 mg, 95% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 2.8 Hz, 2H), 7.46 (d, J = 2.4 Hz, 3H), 5.99 - 5.83 (m, 1H), 5.11 (d, J = 10.0 Hz, 1H), 5.00 (d, J = 17.0 Hz, 1H), 3.29 - 3.17 (m, 2H), 2.74 (t, J = 7.4 Hz, 2H), 1.84 - 1.65 (m, 2H), 1.42 - 1.34 (m, 4H), 0.94 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.8, 162.7, 135.6, 129.8, 129.3, 128.6, 128.2, 116.0, 109.8, 31.4,

27.3, 26.4, 25.7, 22.3, 13.9; IR (KBr)ν_{max}/cm^{-1}: 2927, 2860, 1622, 1447, 1414, 1268, 987, 987, 915, 756, 697; MS (EI) m/z 77, 104, 129, 156, 184, 198, 212, 255; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{17}H_{22}NO$, 256.1696, found 256.1701.

4-Allyl-5-hexyl-3-phenylisoxazole (3bt): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1bt** (121.5 mg, 0.5 mmol) and **2a** (72 mg, 0.6 mmol) afforded **3bt**. R_f = 0.45 (PE/EA = 80: 1); 126 mg, 94% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 - 7.57 (m, 2H), 7.41 (s, 2H), 7.42 (s, 1H), 5.88 (d, J = 9.8, 5.0 Hz, 1H), 5.06 (d, J = 10.8 Hz, 1H), 4.96 (d, J = 17.2 Hz, 1H), 3.20 (d, J = 3.6 Hz, 2H), 2.70 (t, J = 7.4 Hz, 2H), 1.70 (dd, J = 14.4, 7.2 Hz, 2H), 1.40 - 1.28 (m, 6H), 0.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.8, 162.7, 135.6, 129.8, 129.3, 128.6, 128.2, 116.0, 109.8, 31.5, 29.0, 27.6, 26.4, 25.7, 22.5, 14.0; IR (KBr)ν_{max}/cm^{-1}: 2927, 2857, 1621, 1446, 1414, 1383, 1268, 988, 915, 754, 696; MS (EI) m/z 77, 104, 129, 156, 170, 184, 199, 212, 269; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{24}NO$, 270.1852, found 270.1848.

4-(2-Methylallyl)-3,5-diphenylisoxazole (3bu): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1aa** (117.5 mg, 0.5 mmol) and **2b** (88.8 mg, 0.6 mmol) afforded **3bu**. R_f = 0.35 (PE/EA = 80: 1); 133 mg, 97% yield, yellow solid, mp: 106-107 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.0 Hz, 2H), 7.76 - 7.65 (m, 2H), 7.55 - 7.45 (m, 6H), 5.06 (s, 1H), 4.77 (s, 1H), 3.31 (s, 2H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 164.1, 143.1, 129.8, 129.6, 129.5, 128.9, 128.8, 128.3, 126.8, 112.6,

110.7, 31.4, 23.4; IR (KBr)ν_{max}/cm^{-1}: 3067, 2917, 1618, 1446, 1269, 1171, 915, 755, 694; MS (EI) m/z 77, 105, 170, 246, 275; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO$, 276.1383, found 276.1381.

4-(2-Bromoallyl)-3,5-diphenylisoxazole (3bv): Following **Typical Procedure II**, the reaction of $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1aa** (117.5 mg, 0.5 mmol) and **2a** (127.2 mg, 0.6 mmol) afforded **3bv**. R_f = 0.60 (PE/EA = 80: 1); 161 mg, 95% yield, white solid, mp: 107-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (dt, J = 8.2, 2.2 Hz, 2H), 7.70 - 7.61 (m, 2H), 7.54 - 7.41 (m, 6H), 5.63 (dd, J = 18.6, 2.0 Hz, 2H), 3.77 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.6, 163.7, 130.4, 130.3, 130.0, 129.2, 129.0, 128.9, 128.2, 127.6, 126.9, 118.6, 109.3, 36.0; IR (KBr)ν_{max}/cm^{-1}: 2922, 2851, 1613, 1432, 1326, 1175, 1117, 1069, 846, 753, 605, 507; MS (EI) m/z 77, 105, 260, 339; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNO$, 340.0332, found 340.0329.

General Procedure for the Synthesis of Product 4

Typical Procedure III:

Step 1: $Pd(OAc)_2$ (3 mol %, 3.375 mg), *n*-Bu_4NBr (1.0 equiv, 161 mg), DMF (1.0 mL), **1aj** (0.5 mmol), and **2** (0.6 mmol) were added into a test tube successively, and stirred at 80 °C (oil bath) under open air.

Step 2: Upon full consumption of the starting materials detected by TLC, P(*o*-tolyl)$_3$ (12 mg, 0.04 mmol) and Et_3N (5 mL) were added to the solution, and then stirred at reflux (oil bath) under N_2 atmosphere for 3 h, the reaction mixture was filtered through a thin pad of Celite and washed with $CHCl_3$. The filtrate was washed with

HCl, H_2O and brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel to afford **4** as a yellow oil. R_f = 0.30 (PE/EA = 80: 1); (64 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 7.0 Hz, 2H), 7.48 (ddd, J = 19.8, 14.0, 7.0 Hz, 4H), 7.36 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 6.61 (d, J = 10.0 Hz, 1H), 6.17 (dt, J = 10.0, 6.8 Hz, 1H), 3.39 (d, J = 6.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 164.5, 161.8, 139.1, 130.5, 130.0, 129.6, 129.0 128.7, 128.6, 128.3, 128.1, 127.2, 126.9, 119.7, 112.6, 33.6. IR (KBr)ν_{max}/cm^{-1}: 3668, 3311, 2927, 2422, 1562, 1382, 1269, 922, 755; MS (EI) m/z 77, 105, 154, 230, 259; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{14}NO$, 260. 1070, found, 260.1065.

Supporting Information

Copies of the ^{1}H NMR and ^{13}C NMR spectra for all compounds are available in the supporting Information.

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