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Copper-catalyzed oxidative cyclization of chalcone and benzylic amine leading to 2,5-diaryl oxazoles via carbon–carbon double bond cleavage

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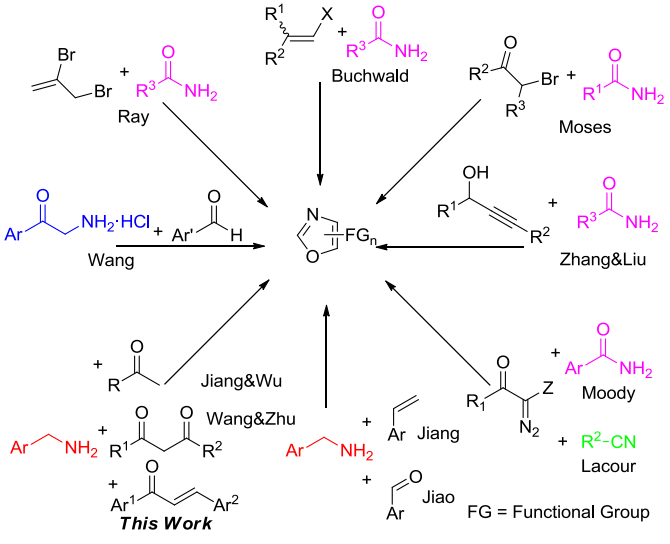
ABSTRACT

A copper-catalyzed oxidative cyclization of chalcone with benzylic amine is achieved, providing 2,5-diaryl oxazoles in moderate to good yields. The procedure employs O_2 as a clean oxidant and involves an oxidative cleavage of the C=C bond as the key step.

1. Introduction

Oxazoles are widely found in natural occurring compounds,[1–4] and pharmaceutical active small molecules.[5,6] Moreover, this framework is also a useful synthetic building block in organic synthesis.[7–14] Hence, many strategies have been developed for the synthesis of oxazole derivatives. Among these strategies, undoubtedly, the direct intermolecular annulation of acyclic precursors to polysubstituted oxazoles from readily available materials is more attractive for the diversity of target molecules in comparison with the traditional intramolecular annulation, such as the Robinson reaction.[15,16] For example, the Van Leusen reaction[17,18] and Fischer oxazole synthesis[19,20] are powerful tools for the construction of this framework. Despite the straightforward strategy, the strong acidic or basic reaction conditions decrease the tolerance of the functional groups. Recently, Zhang described a mild synthesis of oxazole with this direct annulation strategy, which employs gold-catalyzed [2+2+1] annulation of terminal alkyne, nitrile, and an oxygen donor.[21] This elegant strategy was further developed by Saito, in which the oxazole annulation was mediated by iodine(III).[22] An efficient construction of the oxazole framework using the α-diazocarbonyl compounds was developed by Lacour and Moody, respectively.[23–25]

Employing α-aminoketones, Wang reported an iodine-catalyzed tandem oxidative cyclization of 2-amino-1-phenylethanone hydrochloride and aldehyde toward 2,5-disubstituted oxazole (Scheme 1).[26] The participation of carboxamides could also be



Scheme 1. The selected recent reports on the intermolecular annulation leading to oxazole.

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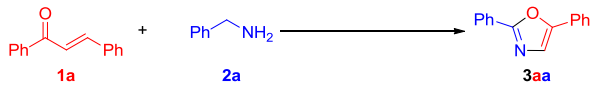
utilized in the construction of oxazole motifs, and several independent reports from Zhan,[27] Liu,[28] Moses,[29] Ray,[30] and Buchwald are depicted in Scheme 1.[31] Meanwhile, benzylamine was wildly employed as commercially available material in the construction of oxazole framework. For example, either the copper-catalyzed or metal-free tandem oxidative cyclization from benzylamine or 1,3-diketone has been reported by Wang and Zhu, respectively (Scheme 1).[32,33] In 2010, Jiang described a TBHP/I_2-mediated domino oxidative cyclization of aryl alkene and benzylic amine toward a polysubstituted oxazole (Scheme 1).[34] In 2012, Jiao reported a copper-mediated aerobic oxidative annulation of aldehyde and benzylamine in the synthesis of oxazole (Scheme 1).[35] In 2013, Jiang and Wu independently described an I_2-promoted annulation of acetophenone and benzylic amine to construct 2,5-disubstituted oxazole (Scheme 1).[36]

Although great progress has been made in the construction of oxazole framework, the development of annulation of benzylamine with readily available starting material involving new type of bond cleavage remains urgent and necessary, one such example develops an annulation of benzylamine with readily available starting material involving new type of bond cleavage. (*E*)-Chalcone is a readily available reagent either from commercially sources or through laboratory condensation of acetophenone and aldehyde. Herein, we report a copper-catalyzed oxidative cyclization of benzylamine and chalcone via carbon–carbon double bond cleavage, which employs O_2 as a clean oxidant leading to 2,5-diaryl oxazole.

2. Result and discussion

We started the cyclization of chalcone and benzylamine in the presence of CuBr, pyridine, and K_2CO_3 in toluene at 110 °C under O_2. The desired oxazole **3aa** was isolated in 5% yield (entry 1, Table 1). To our delight, in the presence of 2.5 equiv of LiBr, the yield was dramatically increased to 63% (entry 2, Table 1). Replacing CuBr with CuCl, $CuCl_2$ and $Cu(OAc)_2$ decreased the yield (entries 3–5, Table 1). Gratifyingly, 78% yield was obtained when $CuBr_2$ was used as catalyst (entry 6, Table 1). The yield dramatically decreased if O_2 was replaced with air or N_2. Conducting the reaction in xylene, $ClCH_2CH_2Cl$ or dioxane (entries 7–9, Table 1) either resulted to low yield or no reaction at all. Further studies revealed that *t*-BuOK and Na_2CO_3 were inferior to K_2CO_3 as the base (entries 10 and 11, Table 1). The employment of LiCl and KBr also resulted in low yields for this transformation (entries 12 and 13, Table 1).

Table 1
Selected results of screening the optimal conditions

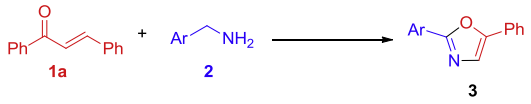


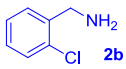
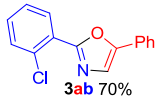
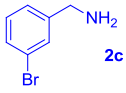
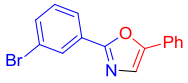
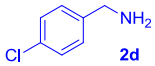
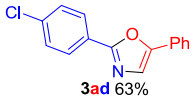
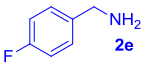
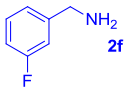
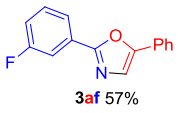
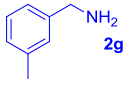
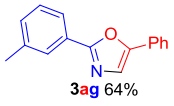
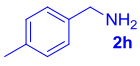
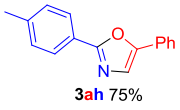
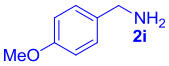
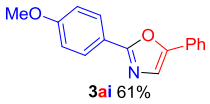
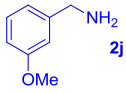
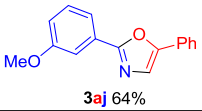
Entry	Copper	Additive	Base	Solvent	Yield[a] (%)
1	CuBr		K_2CO_3	Toluene	5
2	CuBr	LiBr	K_2CO_3	Toluene	63
3	CuCl	LiBr	K_2CO_3	Toluene	35
4	$CuCl_2$	LiBr	K_2CO_3	Toluene	40
5	$Cu(OAc)_2$	LiBr	K_2CO_3	Toluene	8
6	$CuBr_2$	LiBr	K_2CO_3	Toluene	78 (63)[b] (13)[c]
7	$CuBr_2$	LiBr	K_2CO_3	Xylene	52
8	$CuBr_2$	LiBr	K_2CO_3	$ClCH_2CH_2Cl$	0
9	$CuBr_2$	LiBr	K_2CO_3	Dioxane	0
10	$CuBr_2$	LiBr	*t*-BuOK	Toluene	21
11	$CuBr_2$	LiBr	Na_2CO_3	Toluene	48
12	$CuBr_2$	LiCl	K_2CO_3	Toluene	33
13	$CuBr_2$	KBr	K_2CO_3	Toluene	18

[a] Reaction conditions: **1a** (0.2 mmol), benzylamine **2a** (0.4 mmol), $CuBr_2$ (20 mol %), pyridine (0.4 mmol), K_2CO_3 (0.1 mmol), LiBr (0.5 mmol) in dry toluene (2 mL), 110 °C, 11 h, under O_2.
[b] Air.
[c] N_2.

Under the optimized reaction conditions, the scope of benzylamine derivatives was explored, as shown in Table 2.. All substrates including *ortho*, *meta*, and *para* substituted benzylamines ran smoothly, affording the annulation products in moderate to good yields. The reactions seemed not sensitive to the hindrance of *ortho*-substitution of benzylamine (entry 1). Notably, the chloro and bromo groups survived under the reaction conditions, which provided handles for further functionalization.

Table 2
The scope of benzylic amine[a]

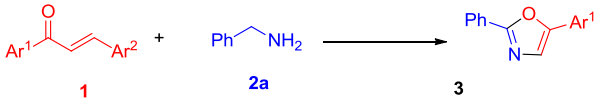


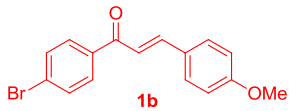
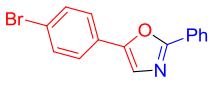
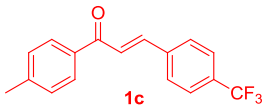
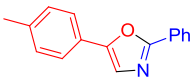
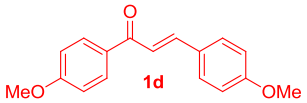
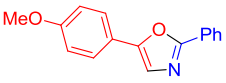
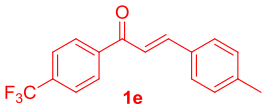
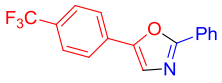
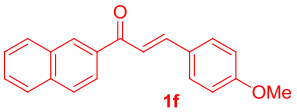
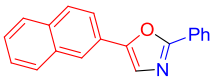
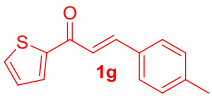
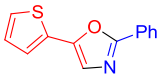
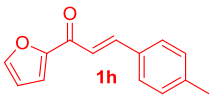
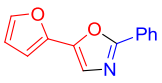
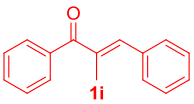
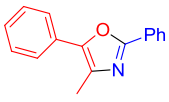
Entry	2	3
1		 **3ab** 70%
2		 **3ac** 61%
3		 **3ad** 63%
4		 **3ae** 60%
5		 **3af** 57%
6		 **3ag** 64%
7		 **3ah** 75%
8		 **3ai** 61%
9		 **3aj** 64%

[a] Reaction conditions: **1a** (0.2 mmol), benzylic amine **2** (0.4 mmol), $CuBr_2$ (20 mol %), pyridine (0.4 mmol), K_2CO_3 (0.1 mmol), LiBr (0.5 mmol) in dry toluene (2 mL), 110 °C, 11 h, under O_2.

Next, the substrate scope of chalcone derivatives was studied. Once again, the cyclization ran smoothly with tolerance of functional groups, such as bromo and trifluoromethyl. Notably, both phenyl groups in chalcone could be substituted and still remain good reactivity in the cyclization. (Table 3). Particularly, the chalcone derivatives with heteroaryl attached in the carbonyl group, such as **1g** and **1h**, provided the oxazoles in 58% and 31% yields,

Table 3
The scope of chalcone derivatives[a]

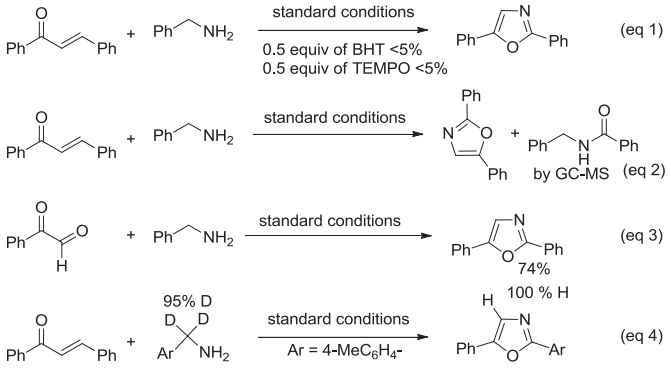


Entry	Substrate **1**	Product **3**
1	 **1b**	 **3ba** 75%
2	 **1c**	 **3ca** 47%
3	 **1d**	 **3da** 64%
4	 **1e**	 **3ea** 68%
5	 **1f**	 **3fa** 82%
6	 **1g**	 **3ga** 58%
7	 **1h**	 **3ha** 31%
8	 **1i**	 **3ia** < 5%

[a] Reaction conditions: **1** (0.2 mmol), benzylic amine **2a** (0.4 mmol), $CuBr_2$ (20 mol %), pyridine (0.4 mmol), K_2CO_3 (0.1 mmol), LiBr (0.5 mmol) in dry toluene (2 mL), 110 °C, 11 h, under O_2.

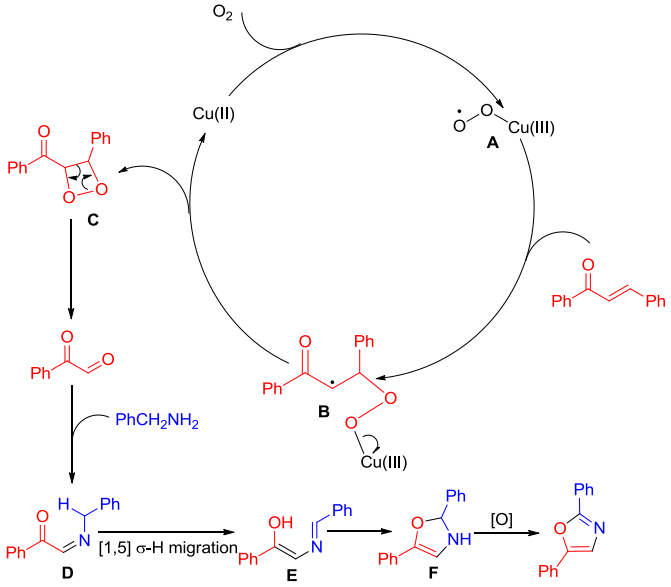
respectively. However, **1i** bearing an α-methyl substitution did not work under this procedure.

The radical scavengers, such as 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and 2,6-di-*tert*-butyl-*p*-methyl phenol (BHT), inhibited the annulation reaction (Scheme 2, Eq. 1), indicating a radical intermediate may be involved in this cyclization. During the reaction, *N*-benzylbenzamide was detected as a by-product (Scheme 2, Eq. 2). When 2-oxo-2-phenylacetaldehyde was subjected to the procedure, **3aa** was isolated in a comparable 74% yield (Scheme 2, Eq. 3). These results revealed 2-oxo-2-phenylacetaldehyde may act as the intermediate for this annulation. Thus, this procedure may involve a C=C bond cleavage leading to 2-oxo-2-phenylacetaldehyde and benzaldehyde. Benzaldehyde and benzylamine further condensed to *N*-benzylbenzamide as by-product.[37–40] Replacing $ArCH_2NH_2$ with $ArCD_2NH_2$ (Ar=4-MeC_6H_4–) afforded no deuterium atom in the oxazole product (Scheme 2, Eq. 4).



Scheme 2. The mechanism study.

Based on these observations, a tentative mechanism is illustrated in Scheme 3. Firstly, the oxidation of Cu(II) by O_2 via a single electron transferring (SET) process produces a Cu(III) species **A**.[41,42] Then, the intermediate **B** is formed by the addition of A to the enone. Secondly, an intramolecular SET followed by the cyclization takes place to form four-membered intermediate **C**, along with a regeneration of Cu(II) species to re-enter the catalytic cycle. Subsequently, the intermediate **C** decomposes to 2-oxo-2-phenylacetaldehyde and benzaldehyde.[43,44] Condensation of 2-oxo-2-phenylacetaldehyde with benzylamine produces intermediate **D**, which produces intermediate **E** via [1,5] σ-H migration. It is consistent with the fact that no deuterium atom was incorporated in the annulation of chalcone with 4-$MeC_6H_4CD_2NH_2$ (Scheme 2, Eq. 4). Finally, the cyclization of intermediate **E** forms the intermediate **F**, which is oxidized by Cu(II) and/or O_2 to oxazole. However, the role of LiBr remains unclear at the current stage.



Scheme 3. The proposed mechanism.

3. Conclusions

In conclusion, we developed a new strategy leading to 2,5-diaryl oxazoles from readily available chalcone and benzylic amine. This procedure involves an oxidative C=C bond cleavage using O_2 as a clean oxidant and represents an attractive alternation for the synthesis of oxazoles.

4. Experimental section

4.1. General information

Chemicals were either purchased or purified by standard techniques. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz spectrometer (^{1}H 500 MHz, ^{13}C 125 MHz) with $CDCl_3$ as the solvent at room temperature. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ=0 ppm) or $CHCl_3$ (7.26 ppm). ^{13}C NMR spectra were obtained by using the same NMR spectrometer and were calibrated with $CDCl_3$ (δ=77.00 ppm). Chemical shifts are given in δ relative to TMS, the coupling constants J are given in hertz (Hz). Column chromatography was performed using EM Silica gel 60 (300–400 mesh).

4.2. General procedure to oxazoles from chalcone and benzylic amine

Under O_2, a mixture of chalcone (0.2 mmol), benzylamine (0.4 mmol), $CuBr_2$ (20 mol %), pyridine (0.4 mmol), K_2CO_3 (0.1 mmol), and LiBr (0.5 mmol) in dry toluene (2 mL) was refluxed at 110 °C for 11 h. After the completion of the reaction, as monitored by TLC, the solvent was concentrated under vacuum and the residue was purified by flash column chromatography through silica gel (300–400 mesh) with petroleum ether/EtOAc as eluant to give the desired product.

4.3. Synthesis of deuterated substrates 4–$MeC_6H_4CD_2NH_2$[47]

Compound **4**–$MeC_6H_4CD_2NH_2$ was synthesized by reduction of 4-methylbenzonitrile (0.52 g, 5 mmol) with lithium aluminum deuteride (0.5 g, 5 mmol) in ice cooled dry ether (50 ml). The mixture was refluxed for 4 h before cooling to 0 °C, EtOAc (0.4 mL) was added to dilute the reaction. After filtration, the filter cake was washed with ether, evaporated under vacuum (25 °C) to afford *p*-tolylmethanamine as a colorless oil. The isotopic purity determined by ^{1}H NMR was 95%.

*4.3.1. 2,5-Diphenyloxazole (**3aa**).*[34] Yellow solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.13–8.11 (m, 2H), 7.73–7.72 (m, 2H), 7.51–7.43 (m, 6H), 7.36–7.33 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.1, 151.2, 130.2, 128.8, 128.7, 128.3, 128.0, 127.4, 126.2, 124.1, 123.4.

*4.3.2. 5-(4-Bromophenyl)-2-phenyloxazole (**3ba**, Table 3).*[34] Yellowish solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.11–8.09 (m, 2H), 7.59–7.56 (m, 4H), 7.49–7.45 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.4, 150.3, 132.1, 130.5, 128.8, 127.3, 127.0, 126.4, 125.6, 123.9, 122.3.

*4.3.3. 2-Phenyl-5-(p-tolyl)oxazole (**3ca**, Table 3).*[35] White solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.11–8.09 (m, 2H), 7.61 (d, J=8.5 Hz, 2H), 7.50–7.45 (m, 3H), 7.40 (s, 1H), 7.26–7.24 (m, 2H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 160.8, 151.5, 138.5, 130.2, 129.6, 128.8, 127.5, 126.2, 125.3, 124.2, 122.8, 21.4.

*4.3.4. 5-(4-Methoxyphenyl)-2-phenyloxazole (**3da**, Table 3).*[36] Yellow solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.09 (d, J=8.5 Hz, 2H), 7.66 (d, J=8.5 Hz, 2H), 7.49–7.45 (m, 3H), 7.33 (s, 1H), 6.97 (d, J=9.0 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=160.6, 159.8, 151.3, 130.1, 128.8, 127.6, 126.1, 125.7, 122.0, 120.9, 114.4, 55.4.

*4.3.5. 2-Phenyl-5-(4-(trifluoromethyl)phenyl)oxazole (**3ea**, Table 3).*[45] White solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.14–8.12(m, 2H) 7.82 (d, J=8.0 Hz, 2H), 7.69 (d, J=8.0 Hz, 2H), 7.56 (s, 1H), 7.51–7.49 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=162.0, 149.8, 131.2, 130.7, 130.0 (q, J_{C-F}=32.5 Hz), 128.9, 127.1, 126.5, 125.9 (q, J_{C-F}=3.8 Hz), 125.2, 124.2, 123.9 (q, J_{C-F}=272.5 Hz).

*4.3.6. 5-(Naphthalen-2-yl)-2-phenyloxazole (**3fa**, Table 3).*[34] White solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.18–8.16 (m, 3H), 7.91–7.87 (m, 2H), 7.85–7.74 (m, 2H), 7.55–7.48 (m, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.3, 151.3, 133.4, 133.1, 130.3, 128.8, 128.7, 128.2, 127.8, 127.5, 126.8, 126.5, 126.3, 125.3, 124.0, 122.9, 122.0.

*4.3.7. 2-Phenyl-5-(thiophen-2-yl)oxazole (**3ga**, Table 3).*[36] Greenish solid; δ=8.10–8.08 (m, 2H), 7.50–7.46 (m, 3H), 7.38–7.37 (m, 1H), 7.35–7.34 (m, 1H), 7.31 (s, 1H), 7.11–7.09 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=160.6, 146.8, 130.4, 129.9, 128.8, 127.8, 127.2, 126.3, 125.6, 124.3, 123.1.

*4.3.8. 5-(Furan-2-yl)-2-phenyloxazole (**3ha**, Table 3).*[34] White solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.09–8.08 (m, 2H), 7.47 (d, J=1.5 Hz, 4H), 7.35 (s, 1H), 6.70 (d, J=3.0 Hz, 1H), 6.53–6.52 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=160.7, 143.8, 143.7, 142.9, 130.4, 128.8, 127.2, 126.4, 123.4, 111.6, 107.3.

*4.3.9. 2-(2-Chlorophenyl)-5-phenyloxazole (**3ab**, Table 2).*[26] Yellowish solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.12–8.09 (m, 1H), 7.75–7.74 (m, 2H), 7.55–7.53 (m, 2H), 7.45 (t, J=8.0 Hz, 2H), 7.39–7.34 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=159.0, 151.7, 132.3, 131.3, 131.0, 130.7, 129.0, 128.6, 127.8, 126.9, 126.2, 124.3, 123.2.

*4.3.10. 2-(3-Bromophenyl)-5-phenyloxazole (**3ac**, Table 2).*[35] Yellowish solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.25–8.24 (m, 1H), 8.05–8.03 (m, 1H), 7.73–7.72 (m, 2H), 7.59–7.57 (m, 1H), 7.47–7.44 (m, 3H), 7.37–7.34 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=159.6, 151.7, 133.2, 130.4, 129.2, 129.1, 129.0, 128.7, 127.7, 124.7, 124.3, 123.6, 122.9.

*4.3.11. 2-(4-Chlorophenyl)-5-phenyloxazole (**3ad**, Table 2).*[26] Yellowish solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.04 (d, J=8.5 Hz, 2H), 7.71 (d, J=8.0 Hz, 2H), 7.47–7.44 (m, 5H), 7.32 (t, J=7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=160.2, 151.5, 136.4, 129.1, 129.0, 128.6, 127.8, 127.5, 125.9, 124.2, 123.5.

*4.3.12. 2-(4-Fluorophenyl)-5-phenyloxazole (**3ae**, Table 2).*[35] Yellowish solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.10–8.07 (m, 2H), 7.71–7.69 (m, 2H), 7.45–7.42 (m, 3H), 7.35–7.32 (m, 1H), 7.18–7.14 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=165.0 (d, J_{C-F}=249.5 Hz), 160.3, 151.3, 128.9, 128.4 (d, J_{C-F}=11.5 Hz), 128.3, 127.9, 124.2, 123.8 (d, J_{C-F}=3.3 Hz), 123.4, 116.0 (d, J_{C-F}=22.1 Hz).

*4.3.13. 2-(3-Fluorophenyl)-5-phenyloxazole (**3af**, Table 2).* Yellowish solid, mp: 68–70 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.90 (d, J=8.0 Hz, 1H), 7.80 (d, J=9.5 Hz, 1H), 7.72 (d, J=7.5 Hz, 2H), 7.46 (t, J=7.5 Hz, 4H), 7.36 (t, J=7.5 Hz, 1H), 7.18–7.14 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=162.9 (d, J_{C-F}=244.8 Hz), 159.4, 151.7, 130.5 (d, J_{C-F}=8.1 Hz), 129.0, 128.7, 127.7, 124.3, 123.6, 122.0 (d, J_{C-F}=3.0 Hz), 117.2 (d, J_{C-F}=21.3 Hz), 113.2 (d, J_{C-F}=23.8 Hz); IR (prism, cm^{-1}): 1593, 1543, 1481, 1267, 1191, 940, 791; HRMS calcd for $C_{15}H_{11}FNO$ ($[M+H]^+$): 240.0819; found: 240.0800.

*4.3.14. 5-Phenyl-2-(m-tolyl)oxazole (**3ag**, Table 2).*[26] Yellowish solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.94–7.91 (m, 2H), 7.73 (d, J=7.0 Hz, 2H), 7.47–7.44 (m, 3H), 7.39–7.33 (m, 2H), 7.27 (d, J=7.5 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.3, 151.2, 138.6, 131.1, 128.9, 128.7, 128.4, 128.1, 127.3, 126.8, 124.2, 123.4, 123.4, 21.4.

*4.3.15. 5-Phenyl-2-(p-tolyl)oxazole (**3ah**, Table 2).*[26] Yellowish solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.99 (d, J=8.0 Hz, 2H), 7.69 (d,

J=7.5 Hz, 2H), 7.42 (t, J=7.5 Hz, 3H), 7.33–7.24 (m, 3H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.4, 150.9, 140.6, 129.5, 128.9, 128.3, 128.1, 126.2, 124.7, 124.1, 123.3, 21.5.

*4.3.16. 2-(4-Methoxyphenyl)-5-phenyloxazole (**3ai**, Table 2).*[46] White solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.07–8.04 (m, 2H), 7.72–7.70 (m, 2H), 7.46–7.41 (m, 3H), 7.33 (t, J=8.0 Hz, 1H), 7.00–6.99 (m, 2H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.3, 161.2, 150.7, 128.9, 128.2, 128.2, 128.0, 124.0, 123.2, 120.3, 114.2, 55.4.

*4.3.17. 2-(3-Methoxyphenyl)-5-phenyloxazole (**3aj**, Table 2).*[26] White solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.74–7.70 (m, 3H), 7.65–7.64 (m, 1H), 7.47–7.38 (m, 4H), 7.37–7.33 (m, 1H), 7.03–7.01 (m, 1H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.0, 159.9, 151.3, 130.0, 128.9, 128.6, 128.5, 127.9, 124.2, 123.4, 118.7, 116.8, 110.9, 55.4.

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Supplementary data

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