JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Synthesis of 2,5-Disubstituted Oxazoles and Oxazolines Catalyzed by Ruthenium(II) Porphyrin and Simple Copper Salts

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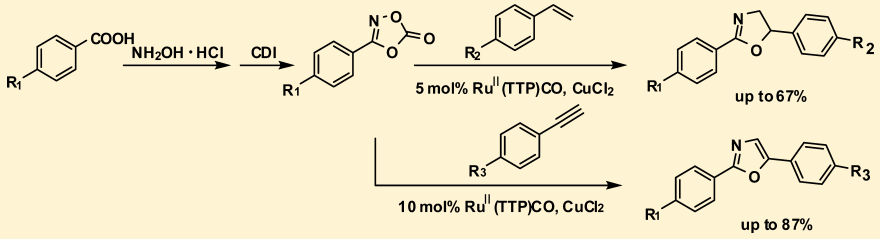
Supporting Information



ABSTRACT: A novel and moderate synthesis of 2,5-disubstituted oxazoles and oxazolines involving ruthenium(II) porphyrin−copper chloride catalyzed cyclization was developed. These reactions using readily available benzene carboxylic acids and phenylethenes or phenylacetylenes are performed under mild conditions. The reactions proceed in series, giving rise to the formation of an intermolecular C−N bond and an intramolecular C−O bond, which yield oxazole or oxazoline derivatives simultaneously.

INTRODUCTION

Oxazoles and oxazolines are attractive heterocyclic compounds not only because of their unique structures and varied applications[1] but also they serve as structural elements for a variety of natural products and pharmaceuticals.[2] Examples of these compounds include Texaline and a tubulin polymerization inhibitor (A-289099), two important antimycobacterial and anticancer agents that comprise 2,5-disubstituted oxazole and oxazoline elements, respectively.[3] Moreover, oxazole and oxazoline derivatives can also be employed as corrosion inhibitors in industrial settings[4] and as chiral ligands in asymmetric synthesis.[5] Because of the important applications of oxazole and oxazoline derivatives, various synthetic methodologies for the production of these compounds have been developed. Generally, oxazole derivatives are synthesized by three typical synthetic methods: cyclization of acyclic precursors,[6] oxidation of oxazolines,[7] and coupling of the prefunctionalized oxazoles with other organometallic reagents.[8] Classical procedures for the synthesis of oxazolines include the thermal cyclization of *N*-(2-hydroxyethyl) amide intermediates[1c] and cyclization prompted by the Burgess reagent,[9] PPh_3/DIAD,[10] DIC/$Cu(OTf)_2$,[11] or DAST/Deoxo-Fluor.[12] The cyclization of *β*-hydroxy carboxylic acid derivatives can also yield the corresponding 1,3-oxazolines under certain conditions.[13] Although some of these reactions allow convenient access to substituted oxazoles and oxazolines, challenges remain, including the limited sources of starting materials and the need to develop milder reaction conditions. In light of these requirements, developing a milder and more general procedure to access substituted oxazoles and oxazolines is simultaneously still desirable. Moreover, the use of benzene carboxylic acids as starting material to give oxazoles and oxazolines has never been reported in the literature.

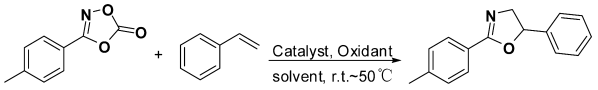
With an interest in identifying an efficient catalyst and an active nitrogen source for the synthesis of new pharmacologically active compounds, we focused on using simple low-cost catalysts and additionally, developing a green transition metal-catalyzed amidation reaction. Among transition metals, copper is particularly attractive in organic synthesis because of its low price, low toxicity, and environmentally benign nature. Thus, copper is gaining favor for use in C−H bond activation[14] and the formation of C−N bonds to yield oxazole derivatives in the presence of the corresponding oxidant.[6c] However, these reactions have low yields of oxazoles and oxazolines when using only simple copper salt as the catalyst. In addition, other materials such as zinc chloride, rhodium chloride, mercuric acetate, and ruthenium(II) porphyrins[15] have been also employed as catalysts for the production of oxazolines. As shown in Table 1, ruthenium(II) porphyrin−copper salt was the most effective catalyst of this reaction due to its high selectivity and efficiency. Herein, we developed a novel ruthenium−copper-catalyzed oxidative cyclization based on easily available benzene carboxylic acids and phenylethenes or phenylacetylenes, providing the substituted oxazoline and oxazole derivatives with moderate yields.

Received: January 13, 2012
Published: March 21, 2012

RESULTS AND DISCUSSION

To initiate our investigate, the reaction of 3-*p*-tolyl-1,4,2-dioxazol-5-one (**1b**) and phenylethene (**2a**) was chosen as a model reaction and was performed in the presence of copper salt, $ZnCl_2$, $Hg(OAc)_2$, $Rh_2(OAc)_4$, or $RhCl_3$ in acetonitrile. Unfortunately, the desired oxazoline products were not obtained. However, the use of Ru(TTP)CO/$CuCl_2$ (or CuCl) as a composite catalyst (Table 1) led to the formation of the desired oxazolines (**3b**). Then the loading of the catalyst was investigated. When the amount of Ru(TTP)CO was increased from 0.02 to 0.05 equiv, the yield increased from 55% to 67% (Table 1, entries 24, 28). Meanwhile, we also found that the amount of $CuCl_2$ had little influence on this reaction when it was decreased from 0.3 to 0.15 equiv (Table 1, entries 28, 30). As a result, the optimal reaction conditions for the synthesis of oxazolines were established as follows: 1.0 equiv of **1** and 5 equiv of **2** as reaction substrates, 0.05 equiv of Ru(TTP)CO and 0.15 equiv of $CuCl_2$ as the catalysts, 0.3 equiv of I_2 as the oxidant, and toluene as the solvent.

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	oxidant	solvent	*T* (°C)	time (h)	yield (%)
1	CuCl		CH_3CN	rt	24	0
2	$CuCl_2$		CH_3CN	rt	24	0
3	$Cu(acac)_2$		CH_3CN	rt	24	0
4	$Cu(CF_3SO_3)_2$		CH_3CN	rt	24	0
5	$ZnCl_2$		CH_3CN	rt	24	0
6	$Hg(OAc)_2$		CH_3CN	rt	24	0
7	$CuCl/Cu(acac)_2$		CH_3CN	rt	24	trace
8	Ru(TTP)CO		CH_3CN	rt	24	trace
9	$Ru_3(CO)_{12}$		CH_3CN	rt	24	0
10	$Rh_2(OAc)_4$		CH_3CN	rt	24	0
11	$RhCl_3$		CH_3CN	rt	24	0
12	Ru(TTP)CO/CuCl		CH_3CN	rt	24	25
13	Ru(TTP)CO/CuCl	MnO_2	CH_3CN	rt	24	trace
14[b]	Ru(TTP)CO/CuCl	O_2	CH_3CN	rt	24	23
15	Ru(TTP)CO/CuCl	I_2	CH_3CN	rt	24	34
16[b]	Ru(TTP)CO/CuCl	I_2/O_2	CH_3CN	rt	24	40
17[b]	Ru(TTP)CO/CuCl	I_2/O_2	CH_3CN	50	3	47
18	Ru(TTP)CO/CuCl	I_2	CH_3CN	50	3	46
19	Ru(TTP)CO/CuCl	I_2	CH_3CN	60	2.5	43
20	Ru(TTP)CO/CuCl	I_2	toluene	50	3	51
21	Ru(TTP)CO/CuCl	I_2	DMF	50	3	trace
22	Ru(TTP)CO/CuCl	I_2	CH_2Cl_2	40	4	28
23	Ru(TTP)CO/CuCl	I_2	1,4-dioxane	50	3	trace
24	Ru(TTP)CO/$CuCl_2$	I_2	toluene	50	3	55
25	Ru(TTP)CO/$Cu(CF_3SO_3)_2$	I_2	toluene	50	3	43
26	Ru(TTP)CO/$Cu(OAc)_2.H_2O$	I_2	toluene	50	3	27
27	Ru(TTP)CO/CuI	I_2	toluene	50	3	49
28[c]	Ru(TTP)CO/$CuCl_2$	I_2	toluene	50	3	67
29[c]	Ru(TTP)CO/$CuCl_2$	I_2	toluene	80	1	55
30[d]	Ru(TTP)CO/$CuCl_2$	I_2	toluene	50	3	66

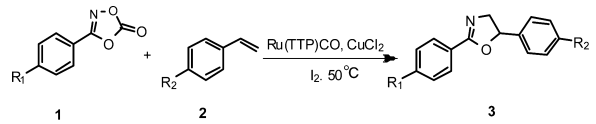
[a]Reaction conditions: **1b** (1.0 equiv, 0.17 mmol), **2a** (4.0 equiv), catalysts [Ru(TTP)CO, 0.02 equiv; copper salts, 0.3 equiv], oxidant (0.3 equiv) in solvent (3 mL). Unless otherwise noted, all reactions were performed under nitrogen. [b]The reaction was carried out in an oxygen atmosphere with 0.3 equiv of iodine. Oxygen is not quantitative. [c]Catalysts: Ru(TTP)CO, 0.05 equiv; copper salt, 0.3 equiv. [d]Catalysts: Ru(TTP)CO, 0.05 equiv; copper salt, 0.15 equiv.

In this work, we also introduced different oxidants into the reaction system to improve the reaction efficiency. It was noted that the addition of MnO_2 made the reaction less efficient (Table 1, entry 13), O_2 made the reaction faster but did not improve the yield (Table 1, entry 14), and I_2 could enhance the reaction yield up to 34% (Table 1, entry 15). In addition, the yield was improved to 40% when we introduced both I_2 and O_2 together as oxidants (Table 1, entry 16).

The reaction temperature also had a great influence on the reaction. Increasing the temperature to 50 °C could shorten the reaction time to 3 h and increase the yield by up to 47% (Table 1, entry 17). Higher temperatures, however, did not result in further improvements (Table 1, entry 19, 29). Meanwhile, we found that O_2 had little influence on the reaction if we raised the temperature (Table 1, entry 18). Subsequently, the reaction solvent was optimized (Table 1, entry 20−23). When acetonitrile was replaced with DMF or 1,4-dioxane, only trace amounts of product were observed (Table 1, entries 21, 23). When the solvent was changed from acetonitrile to dichloromethane, the desired oxazoline was obtained in a lower yield of 28% (Table 1, entry 22). Finally, it was found that toluene was the most suitable solvent for this reaction, as it enhanced the yield to 51% (Table 1, entry 20). With the optimized conditions in hand, the scope of the reaction substrates was investigated. The reactions of some phenylethenes with a series of 3-phenyl-1,4,2-dioxazol-5-one derivatives were investigated. The results are listed in Table 2.

However, the reaction gave the product with a low yield using the phenylacetylenes as the substrate. To further optimize the reaction conditions, we chose the reaction of 3-*p*-tolyl-1,4,2-

Table 2. Synthesis of Oxazolines[a]



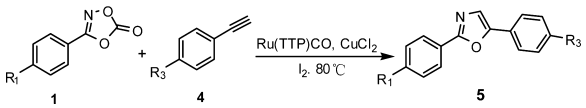
entry	R_1	R_2	oxazolines	yield (%)
1	H	H	**3a**	53
2	Me	H	**3b**	67
3	2-thienyl	H	**3c**	62
4	2-furyl	H	**3d**	72
5	*p*-$C_2H_5OC_6H_4$	H	**3e**	47
6	*p*-$CH_3OC_6H_4$	H	**3f**	50
7	3,4-di-$CH_3OC_6H_4$	H	**3g**	42
8	*p*-ClC_6H_4	H	**3h**	61
9	H	3,4-methylenedioxy	**3i**	49
10	Me	3,4-methylenedioxy	**3j**	65
11	2-thienyl	3,4-methylenedioxy	**3k**	35
12	*p*-$C_2H_5OC_6H_4$	3,4-methylenedioxy	**3m**	67
13	*p*-$CH_3OC_6H_4$	3,4-methylenedioxy	**3n**	55
14	3,4-di-$CH_3OC_6H_4$	3,4-methylenedioxy	**3o**	52
15	Me	Cl	**3p**	60
16	Me	Br	**3q**	56
17	Me	cyclohexene		

[a]Unless otherwise noted, all reactions were carried out with molar ratio of **1**:**2**:Ru(TTP)CO:$CuCl_2$:I_2 = 1:5:0.05:0.15:0.3 at 50 °C for 3−4 h.

dx.doi.org/10.1021/jo202663n | J. Org. Chem. 2012, 77, 4271−4277

dioxazol-5-one (**1b**) and 1-ethoxy-4-ethynylbenzene (**4c**) as the model reaction. In this experiment, it is found that **1b** decomposed too quickly to react with the phenylacetylenes.[16] Thus, we increased the amount of **1b** from 1 to 4 equiv and decreased the amount of **4c** to 1 equiv, which increased the corresponding yield from 35% to 47%. However, we found that the speed of the reaction decreased and the reaction was not complete even after 10 hours. Subsequently, when the reaction temperature was raised to 80 °C, a higher yield of 70% was obtained. The influence of the amount of Ru(TTP)CO was also investigated, and when the loading of Ru(TTP)CO was increased to 0.1 equiv, the yield increased to 87%. Finally, the optimal reaction conditions for the synthesis of oxazoles was obtained: 4.0 equiv of **1** and 1 equiv of **4** as reaction substrates, 0.1 equiv of Ru(TTP)CO and 0.15 equiv of $CuCl_2$ as the catalysts, 0.3 equiv of I_2 as the oxidant, and toluene as the solvent. Under the optimized reaction conditions, the scope of synthesis of oxazoles was explored. The results are shown in Table 3. From these results, we can conclude that this method

Table 3. Synthesis of Oxazoles[a]



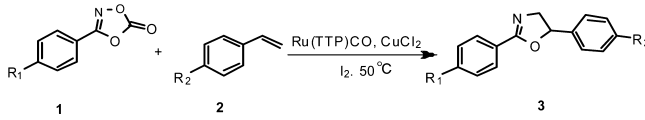
entry	R_1	R_3	oxazoles	yield (%)
1	H	OCH_3	**5a**	82
2	Me	OCH_3	**5b**	49
3	2-thienyl	OCH_3	**5c**	53
4	*p*-$C_2H_5OC_6H_4$	OCH_3	**5d**	46
5	*p*-$(CH_3)_3CC_6H_4$	OCH_3	**5e**	78
6	*p*-ClC_6H_4	OCH_3	**5f**	66
7	H	OC_2H_5	**5g**	75
8	Me	OC_2H_5	**5h**	87
9	2-thienyl	OC_2H_5	**5i**	60
10	*p*-$C_2H_5OC_6H_4$	OC_2H_5	**5j**	57
11	*p*-$(CH_3)_3CC_6H_4$	OC_2H_5	**5k**	78
12	*p*-ClC_6H_4	OC_2H_5	**5l**	52
13[b]	H	H	**5m**	42
14[b]	Me	H	**5n**	55
15[b]	2-thienyl	H	**5o**	73
16[b]	2-furyl	H	**5p**	51
17[b]	*p*-$C_2H_5OC_6H_4$	H	**5q**	80
18[b]	*p*-$CH_3OC_6H_4$	H	**5r**	48
19[b]	3,4-di-$CH_3OC_6H_4$	H	**5s**	23

[a]Unless otherwise noted, all reactions were carried out with the molar ratio of **1**:**4**:Ru(TTP)CO:$CuCl_2$:I_2 = 4:1:0.1:0.15:0.3 at 80 °C for 3−4 h. [b]Reaction conditions: **1**:**4**:Ru(TTP)CO:$CuCl_2$:I_2 = 1:5:0.05:0.15:0.3 at 50 °C for 3−4 h.

provides a convenient method for the preparation of substituted oxazolines and oxazoles from aromatic acids.

To investigate the reaction process, the reaction of 3-phenyl-1,4,2-dioxazol-5-one **1a** was performed in the presence of Ru(TTP)CO, I_2, and using toluene as solvent. After 40−60 min, 3-phenyl-1,4,2-dioxazol-5-one disappeared. Otherwise, the starting material disappeared after at least 4 h without the presence of I_2. On the basis of this finding, we surmise that the main effect is to accelerate the decomposition rate of 3-*p*-tolyl-1,4,2-dioxazol-5-one, making it faster in the conversion into reactive intermediates **A** in the presence of 0.3 equiv of iodine in the reaction process, thereby shortening the reaction time, improve the reaction efficiency. On the other hand, $CuCl_2$ play a role in the compound **B** to compound **3a** conversion process (Scheme 1).

Scheme 1. Synthesis of the Active Intermediate B



To further explore the reaction mechanism of phenyl (2-phenylaziridin-1-yl) methanone **B** to oxazolines **3a**, the active intermediate **B** was synthesized by literature methods.[17] With 2-amino-2-phenylethanol as a substrate, the tandem condensation of esterification−cyclization in $ClSO_3H$ and NaOH system afforded corresponding 2-phenylaziridine. Then the acylation of 2-phenylaziridine was carried out with benzoyl chloride to give the active intermediate **B**. Subsequently, we found that **B** can be translated to forecast product **3a** smoothly at 50 °C by using $CuCl_2$ (0.15 equiv) as catalyst and 0.3 equiv of I_2 as oxidant in toluene. Besides, through LC-MS, we found that **B** exists in the reaction mixture of **1a** and phenylethene. On the basis of the experimental results and previous reports,[16,17b,18] a tentative mechanism was proposed as shown in Scheme 2. First, the intermediate **A** was formed from **1a** via a thermal decomposition and iodine making it faster into reactive intermediates **A** with the release of CO_2 in the reaction process. Second, intermolecular nitrogen atoms transferred from ruthenium imido complexes to styrene and phenylethyne derivatives. Thus the reaction of **A** with styrene derivatives (or phenylethyn-1-ide) generates acylaziridine **B** (or **B′**). Third, isomerization allows the interaction of $CuCl_2$ with the unshared electrons of the amido nitrogen to form **C** (or **C′**), **C** (or **C′**) is unstable and followed rearrangement by the formation of the carbonium ion **D** (or **D′**) and subsequent cyclization by the oxygen to give the oxazolinium salt **E** (or **E′**). Finally, with the regeneration of $CuCl_2$, **E** (or **E′**) gave the 2,5-disubstituted oxazolines **3a** (or oxazoles **5m**).

CONCLUSION

In conclusion, a more moderate synthesis of 2,5-disubstituted oxazolines and oxazoles was developed using a transition-metal ruthenium−copper-catalyzed tandem process for the first time. Further study of the asymmetric synthesis of oxazolines using chiral ruthenium porphyrin catalysts or chiral copper−ligands is underway and will be reported in due course.

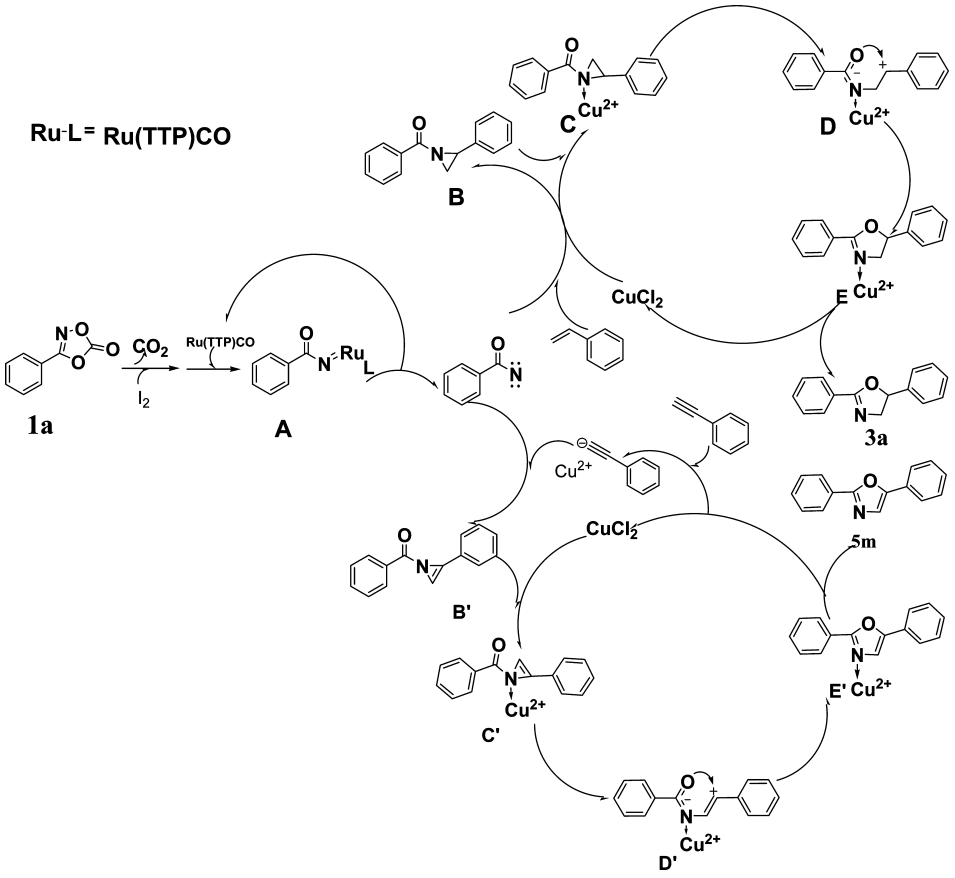
EXPERIMENTAL SECTION

General Information. NMR experiments were recorded on a 400 MHz spectrometer. Column chromatography was performed on silica gel H (300−400 mesh). All reactions were carried out under a nitrogen atmosphere. The substrates **1** were synthesized in one-pot reaction from the corresponding carboxylic acids following a published procedure.[19] The catalyst Ru(TTP)CO was prepared from $Ru_3(CO)_{12}$.[20]

General Procedure for Preparation of 2,5-Disubstituted Oxazolines 3a−3q and Oxazoles 5m−5s. To a solution of phenylethene or ethynylbenzene (0.6 mmol, 4 equiv) in dried toluene (3 mL) was added substrate **1** (0.15 mmol, 1 equiv), Ru(TTP)CO (0.0075 mmol, 5.7 mg), $CuCl_2$ (0.023 mmol, 3.9 mg), and iodine (0.045 mmol, 11.4 mg) simultaneously under a nitrogen atmosphere at room temperature. Then the mixture was stirred at 50 °C for 3−4 h. On completion of the reaction, as indicated by TLC, the reaction

dx.doi.org/10.1021/jo202663n | J. Org. Chem. 2012, 77, 4271−4277

Scheme 2. Tentative Reaction Mechanism



mixture was directly purified by flash column chromatography of silica gel H with petroleum ether and ethyl acetate as eluant to give the final product.

*2,5-Diphenyl-4,5-dihydrooxazole (**3a**; Table 2, Entry 1).*[21] Eluent petroleum ether/ethyl acetate (12:1). Yield, 18 mg, 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−8.05 (m, 2H), 7.32−7.53 (m, 8H), 5.68 (dd, J = 8.0, 10.0 Hz, 1H), 4.50 (dd, J = 10.0, 14.8 Hz, 1H), 4.01 (dd, J = 8.0, 14.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 141.0, 131.5, 128.8, 128.4, 128.3, 128.3, 127.5, 125.7, 81.0, 63.0. HRMS (ESI) calcd for $C_{15}H_{14}NO$: $[M + H]^+$, 224.1075; found m/z, 224.1073.

*5-Phenyl-2-p-tolyl-4,5-dihydrooxazole (**3b**; Table 2, Entry 2).* Eluent petroleum ether/ethyl acetate (12:1). Yield, 24 mg, 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 2H), 7.33−7.40 (m, 5H), 7.25 (d, J = 8.0 Hz, 2H), 5.65 (dd, J = 8.0, 10.0 Hz, 1H), 4.47 (dd, J = 10.0, 14.8 Hz, 1H), 3.98 (dd, J = 8.0, 14.8 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 141.8, 141.1, 129.1, 128.8, 128.3, 128.2, 125.7, 124.8, 80.9, 63.1, 21.6. HRMS (ESI) calcd for $C_{16}H_{16}NO$: $[M + H]^+$, 238.1232; found m/z, 238.1231.

*5-Phenyl-2-(thiophen-2-yl)-4,5-dihydrooxazole (**3c**; Table 2, Entry 3).* Eluent petroleum ether/ethyl acetate (16:1). Yield, 21 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 3.2 Hz, 1H), 7.48(d, J = 4.8 Hz, 1H), 7.32−7.41 (m, 5H), 7.10 (dd, J = 4.0, 4.8 Hz, 1H), 5.66 (dd, J = 8.0, 10.0 Hz, 1H), 4.46 (dd, J = 10.0, 14.8 Hz, 1H), 3.97 (dd, J = 8.0, 14.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 140.5, 130.4, 130.1, 130.0, 128.8, 128.4, 127.6, 125.7, 81.5, 63.1. HRMS (ESI) calcd for $C_{13}H_{12}NOS$: $[M + H]^+$, 230.0640; found m/z, 230.0634.

*2-(Furan-2-yl)-5-phenyl-4,5-dihydrooxazole (**3d**; Table 2, Entry 4).* Eluent petroleum ether/ethyl acetate (7:1). Yield, 23 mg, 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.34−7.39 (m, 5H), 7.02 (d, J = 3.2 Hz, 1H), 6.51 (q, J = 1.6 Hz, 1H), 5.63 (dd, J = 8.0, 10.0 Hz, 1H), 4.47 (dd, J = 10.0, 14.8 Hz, 1H), 4.00 (dd, J = 8.0, 14.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 145.3, 144.1, 140.3, 128.8, 128.5, 125.9, 114.5, 111.5, 81.3, 62.9. HRMS (ESI) calcd for $C_{13}H_{12}NO_2$: $[M + H]^+$, 214.0868; found m/z, 214.0866.

*2-(4-Ethoxyphenyl)-5-phenyl-4,5-dihydrooxazole (**3e**; Table 2, Entry 5).* Eluent petroleum ether/ethyl acetate (12:1). Yield, 19 mg, 47%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.8 Hz, 2H), 7.34−7.42 (m, 5H), 6.94 (d, J = 8.8 Hz, 2H), 5.65 (dd, J = 8.0, 10.0 Hz, 1H), 4.47 (dd, J = 10.0, 14.8 Hz, 1H), 4.09 (q, J = 6.8 Hz, 2H), 3.97 (dd, J = 8.0, 14.8 Hz, 1H), 1.45 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 161.5, 141.2, 130.0, 128.8, 128.2, 127.2, 125.7, 114.2, 80.9, 63.5, 63.1, 14.7. HRMS (ESI) calcd for $C_{17}H_{18}NO_2$: $[M + H]^+$, 268.1338; found m/z, 268.1332.

*2-(4-Methoxyphenyl)-5-phenyl-4,5-dihydrooxazole (**3f**; Table 2, Entry 6).* Eluent petroleum ether/ethyl acetate (7:1). Yield, 19 mg, 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.8 Hz, 2H), 7.33−7.41 (m, 5H), 6.94 (d, J = 8.8 Hz, 2H), 5.65 (dd, J = 8.0, 10.0 Hz, 1H), 4.46 (dd, J = 10.0, 14.4 Hz, 1H), 3.97 (dd, J = 8.0, 14.4 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 162.1, 141.1, 130.0, 128.8, 128.2, 127.2, 125.7, 113.7, 80.9, 63.0, 55.3. HRMS (ESI) calcd for $C_{16}H_{16}NO_2$: $[M + H]^+$, 254.1181; found, m/z, 254.1185.

*2-(3,4-Dimethoxyphenyl)-5-phenyl-4,5-dihydro-oxazole (**3g**; Table 2, Entry 7).* Eluent petroleum ether/ethyl acetate (5:1). Yield, 18 mg, 42%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 1.6, 8.4 Hz, 1H), 7.57 (s, 1H), 7.33−7.42 (m, 5H), 6.91 (d, J = 8.4 Hz, 1H), 5.66 (dd, J = 8.0, 10.0 Hz, 1H), 4.48 (dd, J = 10.0, 14.8 Hz, 1H), 3.98 (dd, J = 8.0, 14.8 Hz, 1H), 3.94 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 151.7, 148.7, 141.0, 128.8, 128.3, 125.8, 121.8, 120.1, 110.7,110.4, 81.1, 63.0, 56.0, 55.9. HRMS (ESI) calcd for $C_{17}H_{18}NO_3$: $[M + H]^+$, 284.1287; found m/z, 284.1292.

*2-(4-Chlorophenyl)-5-phenyl-4,5-dihydrooxazole (**3h**; Table 2, Entry 8).* Eluent petroleum ether/ethyl acetate (25:1). Yield, 23.6 mg, 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.6 Hz, 2H), 7.36−7.43 (m, 7H), 5.68 (t, J = 8.8 Hz, 1H), 4.49 (dd, J = 10.4, 14.4 Hz, 1H), 4.01 (dd, J = 8.0, 14.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 140.7, 137.6, 130.9, 129.6, 128.8, 128.7, 128.4, 125.7,

dx.doi.org/10.1021/jo202663n | J. Org. Chem. 2012, 77, 4271−4277

81.2, 63.1. HRMS (ESI) calcd for $C_{15}H_{12}ClNO$: $[M + H]^+$, 258.0686; found *m*/*z*, 258.0685.

*5-(Benzo[d][1,3]dioxol-5-yl)-2-phenyl-4,5-dihydrooxazole (**3i**; Table 2, Entry 9).* Eluent petroleum ether/ethyl acetate (8:1). Yield, 19.6 mg, 49%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.2 Hz, 2H), 7.44−7.54 (m, 3H), 6.81−6.86 (m, 3H), 5.99 (s, 2H), 5.60 (dd, J = 8.0, 10.0 Hz, 1H), 4.46 (dd, J = 10.0, 14.8 Hz, 1H), 3.99 (dd, J = 8.0, 14.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 148.2, 147.7, 134.7, 131.5, 128.4, 128.3, 127.5, 119.7, 108.3, 106.2, 101.2, 81.2, 62.9. HRMS (ESI) calcd for $C_{16}H_{14}NO_3$: $[M + H]^+$, 268.0974; found *m*/*z*, 268.0967.

*5-(Benzo[d][1,3]dioxol-5-yl)-2-p-tolyl-4,5-dihydro-oxazole (**3j**; Table 2, Entry 10).* Eluent petroleum ether/ethyl acetate (10:1). Yield, 27.4 mg, 65%; mp 81−82 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 6.78−6.83 (m, 3H), 5.96 (s, 2H), 5.57 (dd, J = 8.0, 10.0 Hz, 1H), 4.42 (dd, J = 10.0, 14.8 Hz, 1H), 3.95 (dd, J = 8.0, 14.8 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 148.2, 147.6, 141.9, 134.9, 129.1, 128.2, 124.7, 119.7, 108.3, 106.2, 101.2, 81.0, 62.9, 21.6. HRMS (ESI) calcd for $C_{17}H_{16}NO_3$: $[M + H]^+$, 282.1130; found *m*/*z*, 282.1129.

*5-(Benzo[d][1,3]dioxol-5-yl)-2-(thiophen-2-yl)-4,5-dihydrooxazole (**3k**; Table 2, Entry 11).* Eluent petroleum ether/ethyl acetate (8:1). Yield, 14.3 mg, 35%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.10−7.12 (m, 1H), 6.81−6.84 (m, 3H), 5.98 (s, 2H), 5.57−5.62 (m, 1H), 4.42 (dd, J = 10.0, 14.8 Hz, 1H), 3.95 (dd, J = 8.0, 14.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 148.2, 147.7, 134.3, 130.4, 130.0, 127.6, 119.8, 111.2, 108.3, 106.2, 101.2, 81.6, 63.0. HRMS (ESI) calcd for $C_{14}H_{12}NO_3S$: $[M + H]^+$, 274.0538; found *m*/*z*, 274.0537.

*5-(Benzo[d][1,3]dioxol-5-yl)-2-(4-ethoxyphenyl)-4,5-dihydrooxazole (**3m**; Table 2, Entry 12).* Eluent petroleum ether/ethyl acetate (5:1). Yield, 31.3 mg, 67%; mp 96−99 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.78−6.83 (m, 3H), 5.96 (s, 2H), 5.55 (dd, J = 8.0, 10.0 Hz, 1H), 4.40(dd, J = 10.0, 14.8 Hz, 1H), 4.07 (q, J = 7.2 Hz, 2H), 3.93 (dd, J = 8.0, 14.8 Hz, 1H), 1.44 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 161.5, 148.1, 147.5, 134.9, 129.9, 119.7, 119.6, 114.1, 108.2, 106.2, 101.1, 80.9, 63.5, 62.9, 14.7. HRMS (ESI) calcd for $C_{18}H_{18}NO_4$: $[M + H]^+$, 312.1236; found *m*/*z*, 312.1244.

*5-(Benzo[d][1,3]dioxol-5-yl)-2-(4-methoxyphenyl)-4,5-dihydrooxazole (**3n**; Table 2, Entry 13).* Eluent petroleum ether/ethyl acetate (5:1). Yield, 24.5 mg, 55%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 6.78−6.83 (m, 3H), 5.97 (s, 2H), 5.55 (dd, J = 8.0, 10.0 Hz, 1H), 4.41 (dd, J = 10.0, 14.8 Hz, 1H), 3.90−3.96 (dd, J = 8.0, 14.8 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 162.1, 148.1, 147.6, 135.0, 130.0, 120.1, 119.6, 113.7, 108.3, 106.2, 101.2, 81.0, 63.0, 55.4. HRMS (ESI) calcd for $C_{17}H_{16}NO_4$: $[M + H]^+$, 298.1079; found *m*/*z*, 298.1071.

*5-(Benzo[d][1,3]dioxol-5-yl)-2-(3,4-dimetho-xyphenyl)-4,5-dihydrooxazole (**3o**; Table 2, Entry 14).* Eluent petroleum ether/ethyl acetate (3:1−2:1). Yield, 25.5 mg, 52%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 1.6, 8.4 Hz, 1H), 7.53 (s, 1H), 6.89 (d, J = 8.4 Hz, 1H), 6.78−6.84 (m, 3H), 5.96 (s, 2H), 5.53−5.58 (m, 1H), 4.40 (dd, J = 10.0, 14.4 Hz, 1H), 3.91−3.96 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 151.7, 148.7, 148.2, 147.7, 134.9, 121.7, 120.2, 119.7, 110.7, 110.4, 108.3, 106.2, 101.2, 81.1, 63.0, 56.0, 55.9. HRMS (ESI) calcd for $C_{18}H_{18}NO_5$: $[M + H]^+$, 328.1185; found *m*/*z*, 328.1181.

*5-(4-Chlorophenyl)-2-p-tolyl-4,5-dihydrooxazole (**3p**; Table 2, Entry 15).* Eluent petroleum ether/ethyl acetate (18:1). Yield, 24.5 mg, 60%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.0 Hz, 2H), 6.24−7.38 (m, 6H), 5.62 (dd, J = 8.0, 10.0 Hz, 1H), 4.47 (dd, J = 10.0, 14.8 Hz, 1H), 3.93 (dd, J = 8.0, 14.8 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.5, 140.6, 132.8, 131.7, 129.4, 128.9, 128.8, 128.0, 127.7, 79.3, 62.7, 21.3. HRMS (ESI) calcd for $C_{16}H_{15}ClNO$: $[M + H]^+$, 272.0842; found *m*/*z*, 272.0835.

*5-(4-Bromophenyl)-2-p-tolyl-4,5-dihydrooxazole (**3q**; Table 2, Entry 16).* Eluent petroleum ether/ethyl acetate (18:1). Yield, 26.6 mg, 56%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 2H), 7.49 (d, J = 8.0 Hz, 2H), 7.20−7.25 (m, 4H), 5.58−5.62 (m, 1H), 4.45 (dd, J = 10.0, 14.8 Hz, 1H), 3.91 (dd, J = 8.0, 14.8 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 142.1, 140.1, 131.9, 129.1, 128.8, 128.2, 127.3, 122.1, 80.2, 62.9, 21.6. HRMS (ESI) calcd for $C_{16}H_{15}BrNO$: $[M + H]^+$, 316.0337; found *m*/*z*, 316.0345.

*2,5-Diphenyloxazole (**5m**; Table 3, Entry 13).*[6a] Eluent petroleum ether/ethyl acetate (25:1). Yield, 13.9 mg, 42%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.11−8.13 (m, 2H), 7.74 (d, J = 7.6 Hz, 2H), 7.44−7.52 (m, 6H), 7.34−7.37 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 151.2, 130.3, 128.9, 128.8, 128.4, 127.9, 127.4, 126.2, 124.2, 123.4. HRMS (ESI) calcd for $C_{15}H_{12}NO$: $[M + H]^+$, 222.0919; found *m*/*z*, 222.0920.

*5-Phenyl-2-p-tolyloxazole (**5n**; Table 3, Entry 14).*[6a] Eluent petroleum ether/ethyl acetate (20:1). Yield, 19.4 mg, 55%; mp 69−71 °C (lit.72−73 °C[6b]). ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.43−7.46 (m, 3H), 7.28−7.36 (m, 3H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 150.9, 140.6, 129.5, 128.9, 128.3, 128.0, 126.2, 124.7, 124.1, 123.3, 21.5. HRMS (ESI) calcd for $C_{16}H_{14}NO$: $[M + H]^+$, 236.1075; found *m*/*z*, 236.1078.

*5-Phenyl-2-(thiophen-2-yl)oxazole (**5o**; Table 3, Entry 15).*[23] Eluent petroleum ether/ethyl acetate (20:1). Yield, 25.2 mg, 73%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 2.8 Hz, 1H), 7.70 (d, J = 7.6 Hz, 2H), 7.42−7.46 (m, 3H), 7.40 (s, 1H), 7.32−7.36 (m, 1H), 7.13−7.15 (dd, J = 4.0, 5.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 150.8, 129.9, 128.9, 128.5, 128.3, 128.0, 127.7, 127.6, 124.1, 123.2. HRMS (ESI) calcd for $C_{13}H_{10}NOS$: $[M + H]^+$, 228.0483; Found *m*/*z*, 228.0484.

*2-(Furan-2-yl)-5-phenyloxazole (**5p**; Table 3, Entry 16).*[6b] Eluent petroleum ether/ethyl acetate (13:1). Yield, 16.2 mg, 51%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 2H), 7.59 (d, J = 0.8 Hz, 1H), 7.42−7.46 (m, 3H), 7.33−7.37 (m, 1H), 7.08 (d, J = 3.6 Hz, 1H), 6.57 (q, J = 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 150.8, 144.4, 142.9, 128.9, 128.6, 127.6, 124.2, 123.2, 111.9, 111.4. HRMS (ESI) calcd for $C_{13}H_{10}NO_2$: $[M + H]^+$, 212.0712; found *m*/*z*, 212.0713.

*2-(4-Ethoxyphenyl)-5-phenyloxazole (**5q**; Table 3, Entry 17).* Eluent petroleum ether/ethyl acetate (15:1). Yield, 31.8 mg, 80%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 7.2 Hz, 2H), 7.41−7.46 (m, 3H), 7.31−7.35 (m, 1H), 6.99 (d, J = 8.8 Hz, 2H), 4.11 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 160.7, 150.6, 128.8, 128.1, 127.9, 126.1, 123.9, 123.2, 120.0, 114.6, 63.5, 14.7. HRMS (ESI) calcd for $C_{17}H_{16}NO_2$: $[M + H]^+$, 266.1181; found *m*/*z*, 266.1186.

*2-(4-Methoxyphenyl)-5-phenyloxazole (**5r**; Table 3, Entry 18).*[6a] Eluent petroleum ether/ethyl acetate (12:1). Yield, 18.1 mg, 48%; mp 95−98 °C (lit. 97−99 °C[6b]). ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.8 Hz, 2H), 7.72 (d, J = 7.2 Hz, 2H), 7.41−7.47 (m, 3H), 7.32−7.35 (m, 1H), 7.01 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 161.2, 150.7, 128.9, 128.2, 127.9, 126.1, 124.0, 123.2, 120.2, 114.2, 55.4. HRMS (ESI) calcd for $C_{16}H_{14}NO_2$: $[M + H]^+$, 252.1025; found *m*/*z*, 252.1018.

*2-(3,4-Dimethoxyphenyl)-5-phenyloxazole (**5s**; Table 3, Entry 19).* Eluent petroleum ether/ethyl acetate (6:1). Yield, 9.7 mg, 23%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.71−7.75 (m, 4H), 7.45−7.48 (m, 3H), 7.35−7.38 (m, 1H), 6.98 (d, J = 8.4 Hz, 1H), 4.02 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 151.0, 150.9, 149.1, 128.9, 128.3, 128.1, 124.1, 123.2, 119.5, 111.0, 110.4, 109.0, 56.1, 56.0. HRMS (ESI) calcd for $C_{17}H_{16}NO_3$: $[M + H]^+$, 282.1130; found *m*/*z*, 282.1131.

General Procedure for Preparation of 2,5-Disubstituted Oxazoles 5a−5l. To a solution of ethynylbenzene (0.12 mmol, 1 equiv) in dried toluene (3 mL) was added substrate **1** (0.48 mmol, 4 equiv), Ru(TPP)CO (0.006 mmol, 4.6 mg), $CuCl_2$ (0.018 mmol, 3.1 mg), and iodine (0.036 mmol, 9.1 mg) simultaneously under a nitrogen atmosphere at room temperature. Then the mixture was stirred at 80 °C for 3−4 h. On completion of the reaction, as indicated by TLC, the reaction mixture was directly purified by flash column chromatography on silica gel H with petroleum ether and ethyl acetate as eluant to give the product.

*5-(4-Methoxyphenyl)-2-phenyloxazole (**5a**; Table 3, Entry 1).*[6a] Eluent petroleum ether/ethyl acetate (30:1). Yield, 24.7 mg, 82%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.07−8.14 (m, 2H), 7.66 (d, J = 8.0 Hz,

dx.doi.org/10.1021/jo202663n | J. Org. Chem. 2012, 77, 4271−4277

2H), 7.47 (s, 3H), 7.38 (s, 1H), 6.98 (d, J = 8.0 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 159.7, 151.3, 130.1, 128.7, 127.5, 126.1, 125.7, 121.9, 120.8, 114.3, 55.3. HRMS (ESI) calcd for $C_{16}H_{14}NO_2$: $[M + H]^+$, 252.1025; found m/z, 252.1026.

*5-(4-Methoxyphenyl)-2-p-tolyloxazole (**5b**; Table 3, Entry 2).*[22] Eluent petroleum ether/ethyl acetate (25:1). Yield, 15.6 mg, 49%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 8.8 Hz, 2H), 7.30 (s,1H), 7.28 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 159.7, 150.9, 140.4, 129.5, 126.1, 125.6, 124.8, 121.8, 120.9, 114.3, 55.4, 21.5. HRMS (ESI) calcd for $C_{17}H_{16}NO_2$: $[M + H]^+$, 266.1181; found m/z, 266.1174.

*5-(4-Methoxyphenyl)-2-(thiophen-2-yl)oxazole (**5c**; Table 3, Entry 3).*[23] Eluent petroleum ether/ethyl acetate (20:1). Yield, 16.4 mg, 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 3.6 Hz, 1H), 7.63 (d, J = 8.8 Hz, 2H), 7.43 (d, J = 5.2 Hz, 1H), 7.27 (s, 1H), 7.12–7.14 (m, 1H), 6.97 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 159.8, 156.1, 150.6, 131.7, 129.6, 128.9, 128.0, 125.8, 122.5, 120.1, 114.8, 55.5. HRMS (ESI) calcd for $C_{14}H_{12}NO_2S$: $[M + H]^+$, 258.0589; found m/z, 258.0582.

*2-(4-Ethoxyphenyl)-5-(4-methoxyphenyl)oxazole (**5d**; Table 3, Entry 4).* Eluent petroleum ether/ethyl acetate (15:1). Yield, 16.3 mg, 46%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.8 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.28 (s, 1H), 6.98 (d, J = 3.2 Hz, 2H), 6.96 (d, J = 3.2 Hz, 2H), 4.10 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 1.45 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 160.6, 159.6, 150.7, 127.7, 125.5, 121.7, 121.0, 120.2, 114.6, 114.3, 63.6, 55.3, 14.7. HRMS (ESI) calcd for $C_{18}H_{18}NO_3$: $[M + H]^+$, 296.1287; found m/z, 296.1290.

*2-(4-tert-Butylphenyl)-5-(4-methoxyphenyl)oxazole (**5e**; Table 3, Entry 5).* Eluent petroleum ether/ethyl acetate (30:1). Yield, 28.8 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.31 (s, 1H), 6.97 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 159.7, 153.4, 151.0, 127.9, 125.9, 125.7, 125.6, 121.8, 120.9, 114.3, 55.3, 34.9, 31.1. HRMS (ESI) calcd for $C_{20}H_{22}NO_2$: $[M + H]^+$, 308.1651; found m/z, 308.1652.

*2-(4-Chlorophenyl)-5-(4-methoxyphenyl)oxazole (**5f**; Table 3, Entry 6).*[24] Eluent petroleum ether/ethyl acetate (30:1). Yield, 22.6 mg, 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.33 (s, 1H), 6.98 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 159.6, 151.6, 136.1, 129.1, 128.0, 127.3, 125.8, 122.0, 120.6, 114.4, 55.4. HRMS (ESI) calcd for $C_{16}H_{13}ClNO_2$: $[M + H]^+$, 286.0635; found m/z, 286.0631.

*5-(4-Ethoxyphenyl)-2-phenyloxazole (**5g**; Table 3, Entry 7).* Eluent petroleum ether/ethyl acetate (30:1). Yield, 23.9 mg, 75%; mp 74–76 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.11 (m, 2H), 7.65 (d, J = 8.4 Hz, 2H), 7.45–7.50 (m, 3H), 7.32 (s, 1H), 6.97 (d, J = 8.4 Hz, 2H), 4.08 (q, J = 6.8 Hz, 2H), 1.45 (t, J = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 159.2, 151.3, 130.1, 128.8, 127.5, 126.1, 125.7, 121.8, 120.6, 114.9, 63.6, 14.8. HRMS (ESI) calcd for $C_{17}H_{16}NO_2$: $[M + H]^+$, 266.1181; found m/z, 266.1173.

*5-(4-Ethoxyphenyl)-2-p-tolyloxazole (**5h**; Table 3, Entry 8).* Eluent petroleum ether/ethyl acetate (25:1). Yield, 29.1 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H), 7.27–7.29 (m, 3H), 6.95 (d, J = 8.4 Hz, 2H), 4.07 (q, J = 6.8 Hz, 2H), 2.41(s, 3H), 1.44 (t, J = 6.8 Hz,3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 159.1, 151.0, 140.3, 129.4, 126.0, 125.6, 124.8, 121.7, 120.7, 114.8, 63.5, 21.5, 14.7. HRMS (ESI) calcd for $C_{18}H_{18}NO_2$: $[M + H]^+$, 280.1338; found m/z, 280.1334.

*5-(4-Ethoxyphenyl)-2-(thiophen-2-yl) oxazole (**5i**; Table 3, Entry 9).* Eluent petroleum ether/ethyl acetate (20:1). Yield, 19.5 mg, 60%; mp 68–71 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 3.2 Hz, 1H), 7.62 (d, J = 8.8 Hz, 2H), 7.43 (d, J = 4.4 Hz, 1H), 7.26 (s, 1H), 7.13 (dd, J = 3.6, 4.8 Hz, 1H), 6.96 (d, J = 8.8 Hz, 2H), 4.08 (q, J = 6.8 Hz, 2H), 1.45 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 156.7, 150.8, 133.9, 130.1, 127.9, 127.2, 125.6, 121.6, 120.3, 114.8, 63.5, 14.7. HRMS (ESI) calcd for $C_{15}H_{14}NO_2S$: $[M + H]^+$, 272.0745; found m/z, 272.0758.

*2,5-Bis(4-ethoxyphenyl)oxazole (**5j**; Table 3, Entry 10).* Eluent petroleum ether/ethyl acetate (15:1). Yield, 21.2 mg, 57%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.27 (s, 1H), 6.94–6.98 (m, 4H), 4.05–4.13 (m, 4H), 1.43–1.47 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 160.5, 159.0, 150.7, 127.7, 125.5, 121.6, 120.9, 120.2, 114.8. 114.6, 63.6, 63.5, 14.8, 14.7. HRMS (ESI) calcd for $C_{19}H_{20}NO_3$: $[M + H]^+$, 310.1443; found m/z, 310.1447.

*2-(4-tert-Butylphenyl)-5-(4-ethoxyphenyl)oxazole (**5k**; Table 3, Entry 11).* Eluent petroleum ether/ethyl acetate (30:1). Yield, 30.3 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.31 (s, 1H), 6.96 (d, J = 8.8 Hz, 2H), 4.07 (q, J = 7.2 Hz, 2H), 1.44 (t, J = 7.2 Hz, 3H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 159.1, 153.4, 151.0, 127.6, 125.9, 125.7, 125.6, 121.7, 120.8, 114.8, 63.5, 34.9, 31.1, 14.7. HRMS (ESI) calcd for $C_{21}H_{24}NO_2$: $[M + H]^+$, 322.1807; found m/z, 322.1802.

*2-(4-Chlorophenyl)-5-(4-ethoxyphenyl)oxazole (**5l**; Table 3, Entry 12).* Eluent petroleum ether/ethyl acetate (30:1). Yield, 18.7 mg, 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.8 Hz, 2H), 7.63 (d, J = 8.8 Hz, 2H), 7.45 (d, J = 8.8 Hz, 2H), 7.31 (s, 1H), 6.96 (d, J = 8.8 Hz, 2H), 4.08 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 159.3, 151.6, 136.1, 129.1, 127.3, 126.0, 125.7, 121.9, 120.4, 114.9, 63.6, 14.8. HRMS (ESI) calcd for $C_{17}H_{15}ClNO_2$: $[M + H]^+$, 300.0791; found m/z, 300.0798.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by the National Science Foundation of China (no. 21072131).

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