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A Divergent Approach to Indoles and Oxazoles from Enamides by Directing-Group-Controlled Cu-Catalyzed Intramolecular C-H Amination and Alkoxylation

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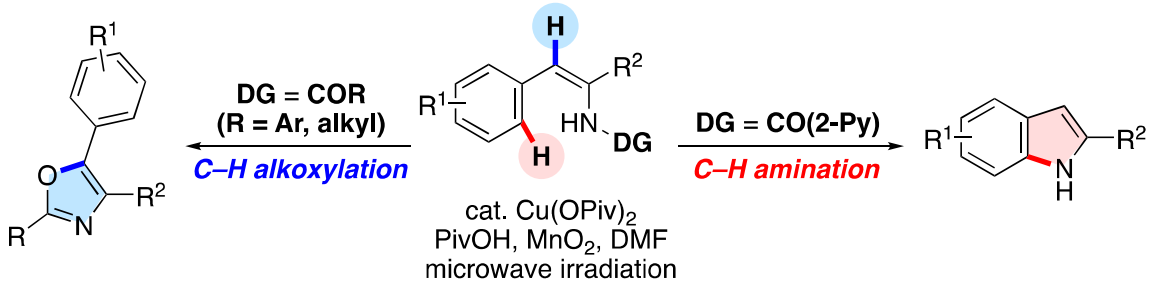


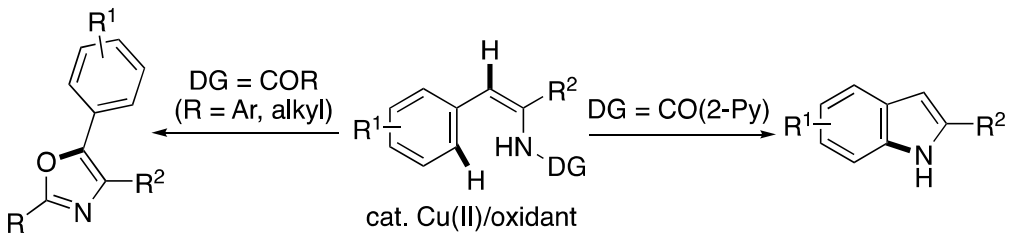
A directing-group-controlled, copper-catalyzed divergent approach to indoles and oxazoles from enamides has been developed. The picolinamide-derived enamides undergo the intramolecular aromatic C–H amination in the presence of a $Cu(OPiv)_2$ catalyst and an MnO_2 oxidant to form the corresponding indoles in good yields. On the other hand, simpler aryl- or alkyl-substituted enamides are converted to the 2,4,5-trisubstituted oxazole frameworks via vinylic C–H alkoxylation under

identical conditions. The copper catalysis can provide uniquely divergent access to indole and oxazole heteroaromatic cores of great importance in medicinal and material chemistry.

Introduction

Nitrogen-containing heteroaromatic rings are prevalent substructures in bioactive molecules, pharmaceutical targets, and functional materials. Synthetic chemists thus have developed many methodologies for the construction of above heterocycles. Among numerous reported procedures, the copper-mediated oxidative cyclization via C–H cleavage now receives significant attention because of its higher synthetic efficiency associated with atom and step economies.[1] Our research group also focused on the unique activity of less toxic, stable, and abundant copper salts and developed several Cu(II)-catalyzed intramolecular C–H amination reactions for the synthesis of carbazoles,[2a] indolines,[2b] and isoindolinones.[2c] As the next reaction design, we envisioned the C–H amination of aryl-substituted enamides: the expected Cu(II)-catalyzed aromatic C–H activation occurs with the aid of picolinamide directing group to form the desired indoles in good yields (Scheme 1, right).[3,4] Additionally, we have serendipitously found that similar aryl- and alkyl-substituted enamides undergo the vinylic C–H alkoxylation under identical conditions, delivering the corresponding 2,4,5-trisubstituted oxazoles selectively (Scheme 1, left).[5] Thus, by the judicious choice of directing group, the single enamide skeleton is divergently converted under the same copper-catalyzed conditions to indole[6] and oxazole[7] of great interest in medicinal chemistry. Such a directing-group-controlled regiodivergent C–H activation was observed in some palladium- or rhodium-based catalysis[8] but still remains underdeveloped under cooper-catalyzed conditions.[2c] The detailed optimization studies and substrate scope are reported herein.

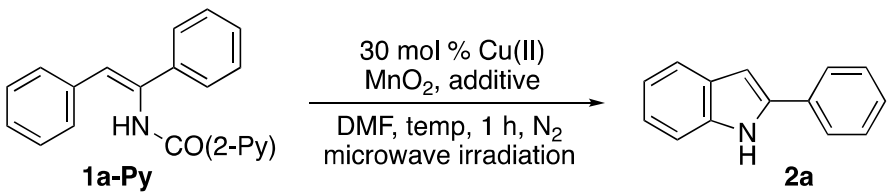
Scheme 1. Directing-Group-Controlled Divergent Approach to Indoles and Oxazoles via Cu-Catalyzed C–H Cleavage



Results and Discussion

On the basis of our previous success of carbazole synthesis,[2a] optimization studies commenced with *N*-picolinoyl enamide **1a-Py** (0.10 mmol; Table 1), which was readily prepared by the CsOH-mediated hydroamidation of phenylacetylene with picolinamide.[9] In an initial experiment, heating a DMF suspension of **1a-Py**, 30 mol % $Cu(OAc)_2$, and 2.0 equiv of MnO_2 under microwave irradiation (180 ˚C, 1 h) afforded the desired 2-phenylindole (**2a**) in 37% GC yield (entry 1). Same as shown in the previous work,[2a] the corresponding *N*-picolinoyl indole was not detected at all, and *NH*-indole **2a** was exclusively formed. After the aqueous workup, we successfully detected the picolinic acid in the aqueous phase by TOF-MS. Thus, the trace water in DMF solvent can promote the spontaneous hydrolysis in situ (vide infra). The addition of AcOH increased the yield to 63% (entry 2). We then tested several acetate-type Cu(II) salts, and bulkier $Cu(OPiv)_2$, $Cu(OCOAd)_2$, and $Cu(eh)_2$ showed better reactivity (entries 3–5). Subsequent screening of acidic additives with $Cu(eh)_2$ identified PivOH to be optimal (entries 6–8). Additional fine tuning revealed that a combination of $Cu(OPiv)_2$ and PivOH was best (entries 9 and 10), and finally 91% isolated yield was obtained at slightly higher temperature (entry 11). No reaction occurred in the absence of $Cu(OPiv)_2$, confirming the copper catalysis in the present transformation (entry 12). Additionally, we also tested other oxidants including AgOAc, $K_2S_2O_8$, and $Mn(OAc)_3$ under otherwise optimal conditions, but the indole **2a** was observed in only <9% GC yield (data not shown).

Table 1. Optimization for Copper-Catalyzed Intramolecular C–H Amination of Enamide 1a-Py for Synthesis of Indole 2a[a]



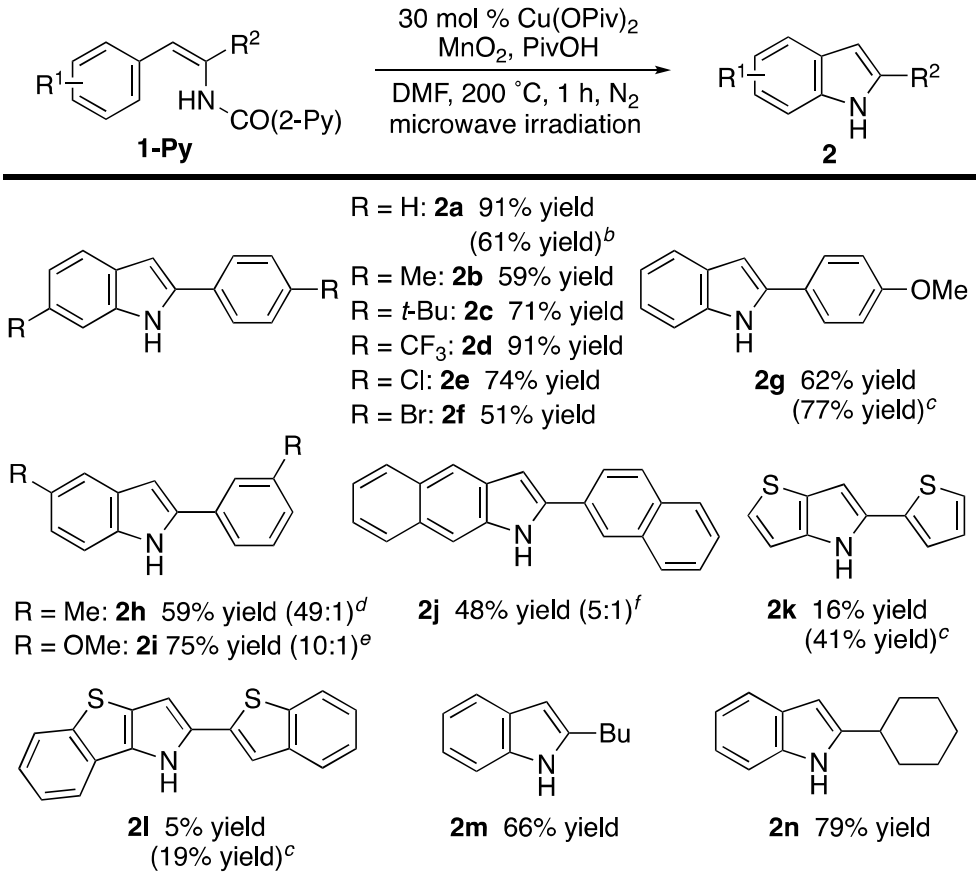
entry	Cu(II)	additive (equiv)	temp (˚C)	yield (%)[b]
1	$Cu(OAc)_2$	none	180	37
2	$Cu(OAc)_2$	AcOH (1.0)	180	63
3	$Cu(OPiv)_2$	AcOH (1.0)	180	69
4	$Cu(OCOAd)_2$	AcOH (1.0)	180	72
5	$Cu(eh)_2$	AcOH (1.0)	180	72
6	$Cu(eh)_2$	EtCOOH (1.0)	180	71
7	$Cu(eh)_2$	PivOH (1.0)	180	77
8	$Cu(eh)_2$	AdCOOH (1.0)	180	52
9	$Cu(eh)_2$	PivOH (1.5)	180	75
10	$Cu(OPiv)_2$	PivOH (1.5)	180	84 (84)
11	$Cu(OPiv)_2$	PivOH (1.5)	200	(91)
12	none	PivOH (1.5)	200	0

[a] Reaction conditions: **1a-Py** (0.10 mmol), Cu(II) (0.030 mmol), MnO_2 (0.20 mmol), additive, DMF (0.60 mL), 1 h, N_2, microwave irradiation. [b] Estimated by GC method. Isolated yield is in parentheses. Ad = 1-adamanthyl, eh = 2-ethyl-1-hexanoate, 2-Py = 2-pyridyl.

Under conditions of entry 11 in Table 1, we performed the aromatic C–H amination of various enamides. The representative indole products are illustrated in Scheme 2. The copper catalysis was compatible with electronically diverse functions including methyl, *tert*-butyl, trifluoromethyl, and methoxy groups, and the corresponding substituted indoles **2b**–**d** and **2g** were obtained in synthetically useful yields. The aromatic C–Cl and C–Br moieties were also tolerated (**2e** and **2f**), which can provide a useful synthetic handle for further manipulations based on the palladium-catalyzed

cross-coupling chemistry.[10] In the cases of *meta*-substituted enamides, the more sterically accessible C–H was preferably aminated (**2h** and **2i**). The same regioselectivity trend was observed in the reaction of 2-naphtyl-substituted enamide (**2j**). On the other hand, thienyl and benzothienyl substrates were somewhat unstable under the standard conditions with the MnO_2 terminal oxidant, but the corresponding thiophene-fused pyrrole rings **2k** and **2l** were obtained by using stoichiometric $Cu(OPiv)_2$ and conventional heating method with an oil bath. The stoichiometric conditions also increased the yield of electron-rich **2g**. In the stoichiometric reactions of theses electron-rich substrates, a small but significant amount of the corresponding *N*-picolinoylindoles was detected by GC and GCMS analysis. However, upon workup with ethylenediamine, the *N*-picolinoyl group was smoothly removed to from the NH indoles exclusively (see the Experimental Section for details). The copper-catalyzed C–H amination also accommodated the primary and secondary alkyl substituents to furnish the 2-alkylindoles in good yields (**2m** and **2n**). The reaction could also be conducted on a preparative scale (1.0 mmol) (**2a**). Although similar intramolecular C–H aminations directed toward indole were already reported,[4] they still relied on precious Pd catalysts or stoichiometric hypervalent I(III) oxidants. The present protocol is the first successful example of indole synthesis via copper-catalyzed C–H amination, to the best of our knowledge.

Scheme 2. Copper-Catalyzed Intramolecular C–H Amination of Various Enamides 1-Py for Synthesis of Indoles 2[a]



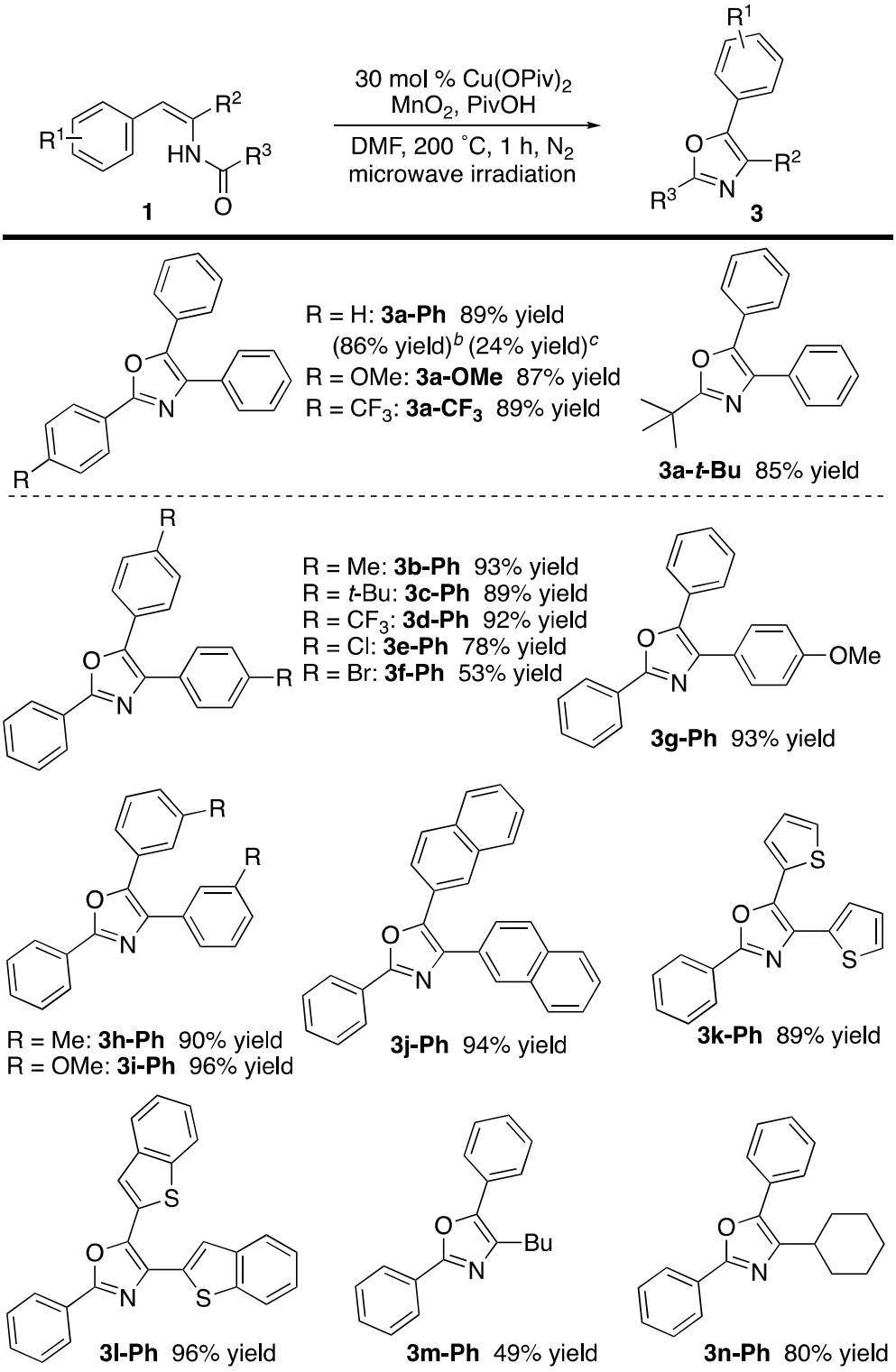
[a] Reaction conditions: **1-Py** (0.10 mmol), Cu(OPiv) (0.030 mmol), MnO_2 (0.20 mmol), PivOH (0.15 mmol), DMF (0.60 mL), 1 h, N_2, microwave irradiation. Isolated yields are shown. [b] 1.0 mmol scale. [c] With 2.0 equiv $Cu(OPiv)_2$ in the absence of MnO_2. At 150 ˚C with an oil bath for 4 h. [d] Regioisomeric ratio. The major isomer **2h** was isolated in 58% yield. [e] Combined isolated yield of regioisomers. Regioisomeric ratio is in parenthesis. [f] Regioisomeric ratio. The major isomer **2j** was isolated in 40% yield.

We next investigated the effect of substituent on enamide nitrogen and serendipitously found that the corresponding *N*-benzoyl enamide **1a-Ph** completely changed the reaction course even under otherwise identical conditions: the intramolecular vinylic C–H alkoxylation proceeded selectively to afford the 2,4,6-triphenyloxazole **3a-Ph** in 89% isolated yield (Scheme 3). Both an electron-donating methoxy and an electron-withdrawing trifluoromethyl groups were well tolerated (**3a-OMe** and **3a-CF_3**), and even *tert*-butyl-substituted enamide was converted to the trisubstituted oxazole in 85% yield (**3a-*t*-Bu**).

Also in this case, the reaction could be easily scaled up to 1.0 mmol (**3a-Ph**). On the other hand, even in the absence of $Cu(OPiv)_2$, a small but significant amount of **3a-Ph** (24% GC yield) was observed.

Prompted by the above intriguing product selectivity switching, we subsequently implemented the reaction of various benzoyl-substituted enamides **1-Ph**. The corresponding triaryloxazoles were uniformly formed with good to excellent yields from a wide range of *para*- and *meta*-substituted enamides (**3b-Ph**–**3i-Ph**). The substrates bearing the sterically demanding naphthyl and heteroaromatic thienyl substituents also underwent the cyclization smoothly (**3j-Ph**–**3l-Ph**). Additionally, the 4-alkyloxazoles were also readily constructed under identical conditions (**3m-Ph** and **3n-Ph**).

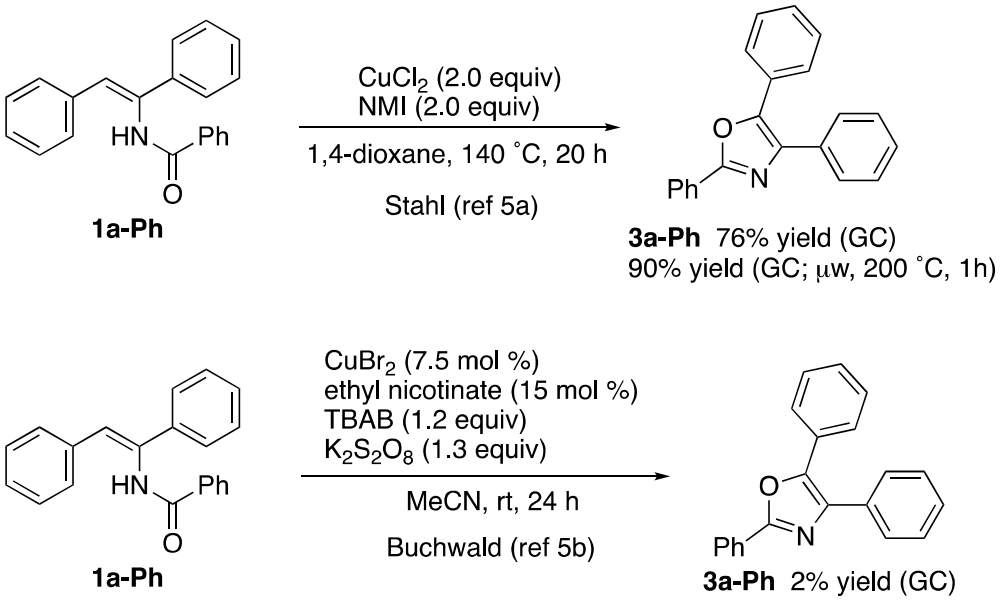
Scheme 3. Copper-Catalyzed Intramolecular C–H Alkoxylation of Enamides 1 for Synthesis of Oxazoles 3[a]



[a] Reaction conditions: **1** (0.10 mmol), Cu(OPiv) (0.030 mmol), MnO_2 (0.20 mmol), PivOH (0.15 mmol), DMF (0.60 mL), 1 h, N_2, microwave irradiation. Isolated yields are given. [b] 1.0 mmol scale. [c] GC yield without $Cu(OPiv)_2$ catalyst.

The related copper-mediated and -catalyzed cyclization of enamides were already developed by Stahl[5a] and Buchwald.[5b] However, only attempts to construct 2,5-disubstituted oxazoles were reported. Thus, we tested the reaction of **1a-Ph** under literature conditions (Scheme 4): the trisubstituted oxazole **3a-Ph** was formed in 76% GC yield under $CuCl_2$-mediated conditions developed by Stahl whereas Buchwald's procedure using a $CuBr_2$ catalyst gave **3a-Ph** in only <2% yield. Under microwave-modified conditions, the $CuCl_2$/NMI system provided **3a-Ph** in 90% GC yield, but a stoichiometric amount of $CuCl_2$ was still necessary. These outcomes demonstrate the synthetic advantage of our newly developed $Cu(OPiv)_2/MnO_2$ catalyst system.

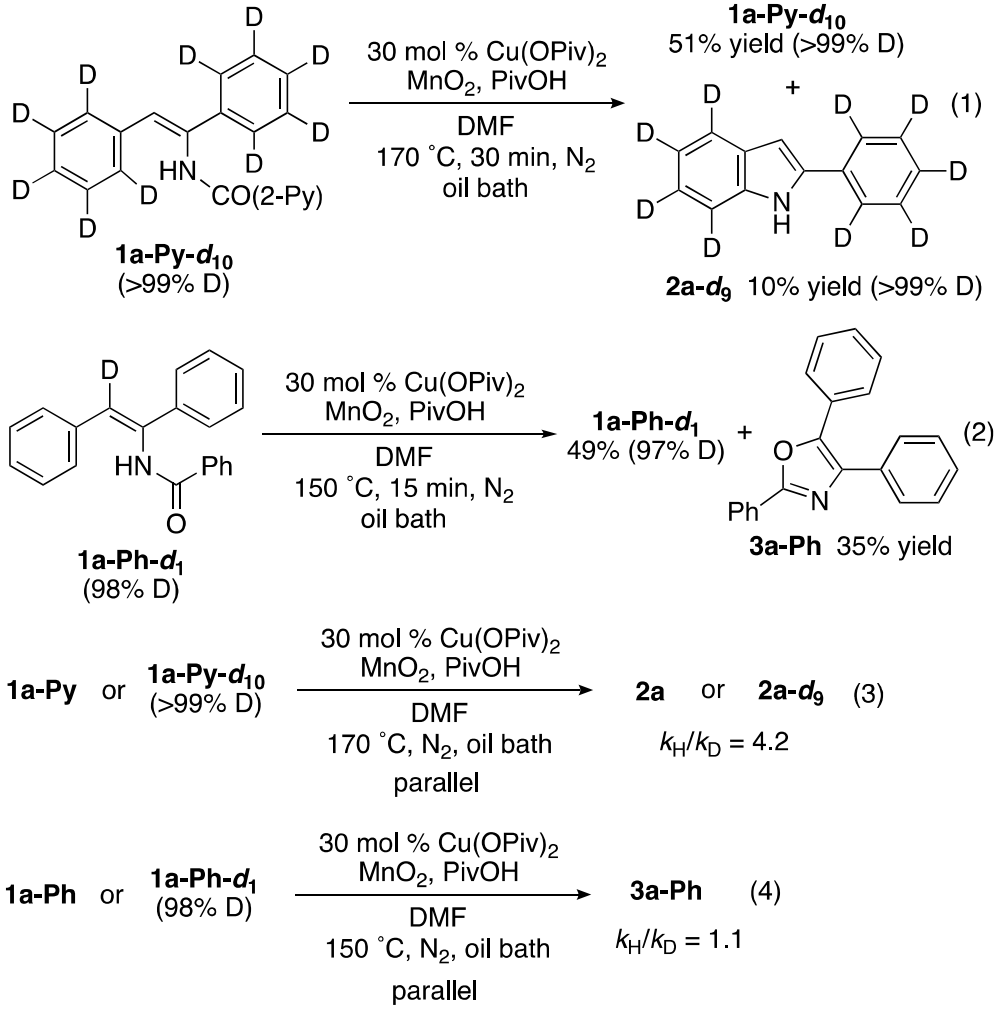
Scheme 4. Attempts to Apply Reported Cu-Promoted Conditions for Synthesis of Oxazole 3a-Ph



To gain some mechanistic insight, several deuterium-labeling experiments with **1a-Py-d_{10}** and **1a-Ph-d_1** were carried out (Scheme 5, see the Supporting Information for more detail). All deuterium-labeling

experiments were performed under the conventional heating conditions with an oil bath, because under microwave-assisted conditions the reaction proceeded in the course of the preheating time up to 200 ˚C, and the conversion at an early stage was difficult to monitor. We initially checked the irreversibility of C–H cleavage. At an early stage of reaction, no H/D exchange occurred in both indole and oxazole formations (eqs 1 and 2). Thus, the kinetic isotope effect (KIE) value of each reaction was investigated: 4.2 and 1.1 were obtained for **1a-Py** and **1a-Ph**, respectively (eqs 3 and 4).

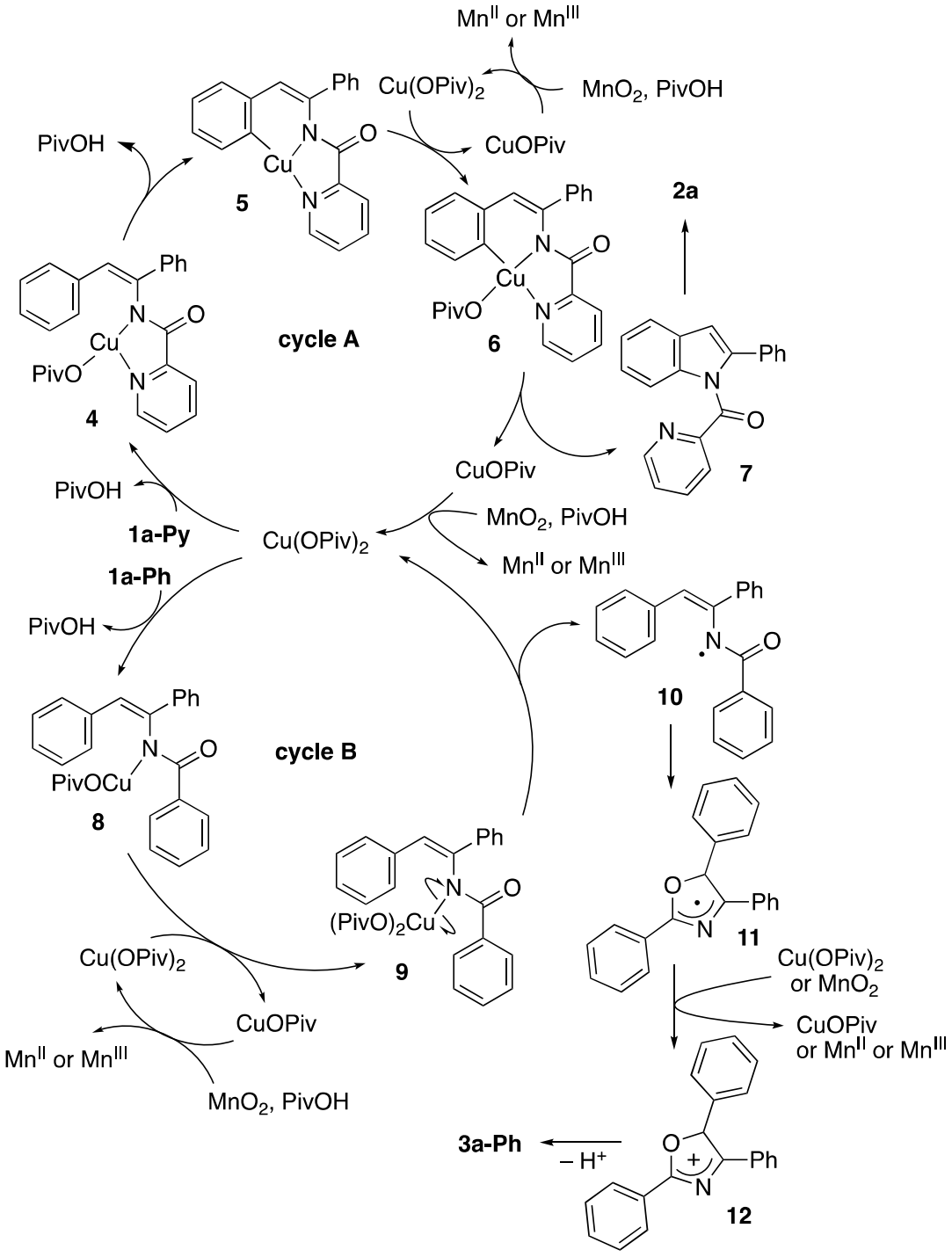
Scheme 5. Deuterium-Labeling Experiments



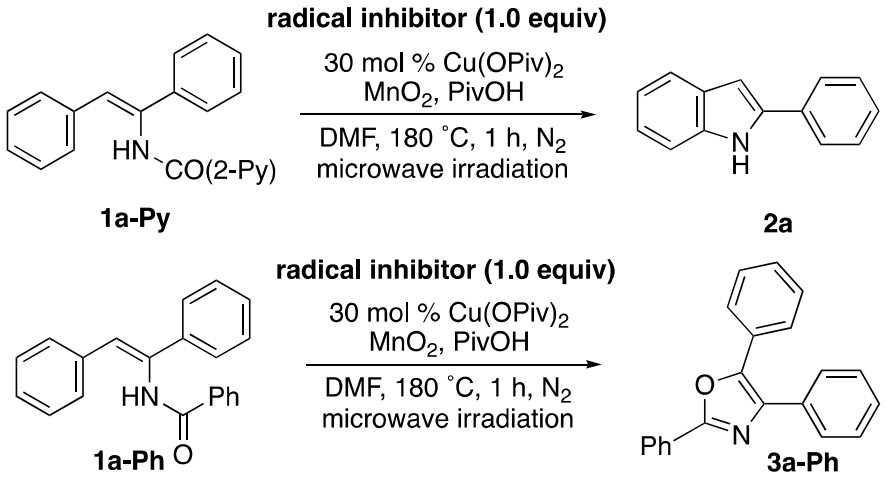
On the basis of the above results and literature information, we are tempted to assume the reaction mechanism of **1a-Py** and **1a-Ph** as follows (Scheme 6). For the formation of indole **2a** (cycle A), the starting $Cu(OPiv)_2$ initially undergoes the ligand exchange with **1a-Py** generates the *N,N*-bidentately

coordinated Cu complex **4**.[11] Subsequent rate-limiting C–H cleavage[12] (**4** → **5**) is followed by disproportionation with additional $Cu(OPiv)_2$ to afford a Cu(III) species **6**.[13] The indole framework **7** is then constructed by reductive elimination from **6**. Spontaneous hydrolysis of **7** in situ gives the observed *NH*-indole **2a**. On the other hand, the formed CuOPiv is reoxidized by MnO_2[14] into $Cu(OPiv)_2$ to complete the catalytic cycle A. On the other hand, the oxazole **3a-Ph** formation process (cycle B) includes (1) ligand exchange with **1a-Ph** ($Cu(OPiv)_2$ ⟶ **8**), (2) disproportionation-induced oxidation into Cu(III) species **9**, and (3) homolysis of the resulting N–Cu(III) bond along with the regeneration of the staring $Cu(OPiv)_2$.[2c,15] The formed amidyl radical **10** undergoes cyclization (**10** ⟶ **11**) followed by the single electron transfer (SET) oxidation (**11** ⟶ **12**) and deprotonation to furnish the oxazole **3a-Ph**. The minor background reaction observed in Scheme 3 suggests less effective but significant oxidation aptitude of MnO_2 for the generation of radical species **11**. However, radical inhibitors, TEMPO and galvinoxyl, did not completely shut down oxazole formation as well as indole formation (Scheme 7). Thus, the initial single electron transfer (SET) oxidation, which was originally proposed by Stahl[5a] is also plausible, and details still remain to be elucidated.[16]

Scheme 6. Plausible Mechanism



Scheme 7. Effects of Radical Inhibitors



inhibitor	GC yield of **2a**
none	84% yield
TEMPO	58% yield
Galvinoxyl	22% yield

inhibitor	GC yield of **3a-Ph**
none	97% yield
TEMPO	92% yield
Galvinoxyl	61% yield

Conclusion

We have developed a copper-catalyzed oxidative cyclization approach to indoles and oxazoles via C–H amination and alkoxylation, respectively. The directing-group-controlled divergent mechanisms, namely Cu(I)/(II)/(III) organometallic pathway and amidyl radical pathway, are operated, and indoles and oxazoles are selectively obtained from enamides of same skeleton. Such a directing-group-controllable strategy enables diversity-oriented synthesis of *N*-heterocycles through multisite-selective C–H functionalization. Further development of related regioselective and/or -divergent Cu catalysts is ongoing and will be reported in due course.

Experimental Section

Instrumentation and Chemicals ^{1}H, $^{13}C\{^{1}H\}$, and $^{19}F\{^{1}H\}$ NMR spectra were recorded at 400 MHz, 100 MHz, and 376 MHz, respectively, for $CDCl_3$ or DMSO-d_6 solutions. HRMS data were obtained by APCI using TOF. GC analysis was carried out using a silicon OV-17 column (2.6 mm i.d. x 1.5 m) or a CBP-1 capillary column (0.5 mm i.d. x 25 m). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck silica gel $60F_{254}$. Silica gel (Wakosil C-200) was used for column chromatography. Gel permeation chromatography (GPC) was performed by LC-6AD (pump, SHIMADZU, 3.5 mL/min $CHCl_3$) and SPD-20A (UV detector, SHIMADZU, 254

nm) with two in-line GPC H-2001 (20 x 500 mm, particle size: 15 μm) and H-2002 columns (20 x 500 mm, particle size: 15 μm) (preparative columns, Shodex, $CHCl_3$ eluent) or by LC-20AR (pump, SHIMADZU, 7.5 mL/min EtOAc) and SPD-20A (UV detector, SHIMADZU, 254 nm) with two in-line YMC-GPC T2000 (20 x 600 mm, particle size: 10 μm) (preparative columns, YMC, EtOAc eluent). Microwave irradiation was conducted with Initiator$^+$ (Biotage), and the reaction temperature was measured by an internal probe. Unless otherwise noted, materials obtained from commercial suppliers were used as received. $Cu(OPiv)_2$ was prepared according to the literature.[17] DMF was dried on a Glass Contour Solvent dispensing system (Nikko Hansen & Co., Ltd.) prior to use. Enamides **1**, except for **1g-Py** and **1g-Ph**, were synthesized by the CsOH-mediated hydroamidation of corresponding internal alkynes and benzamides.[9] Conventional condensation was conducted for the preparation of **1g-Py** and **1g-Ph**.[18] All reactions were carried out under nitrogen atmosphere unless otherwise noted.

Preparation of 1a-Ph-d_1. In a glovebox filled with nitrogen, diphenylacetylene (67 mg, 0.38 mmol), benzamide (45 mg, 0.38 mmol), and $CsOH•OH_2$ (63 mg, 0.38 mmol) were placed in a 2.0 mL microwave vessel. The vessel was sealed with a cap and then taken out of the glovebox. Dimethyl sulfoxide-d_6 (DMSO-d_6, 1.5 mL) was sequentially injected via a syringe. The mixture was stirred for 24 h at 120 °C. The resulting mixture was then quenched with water. The mixture was extracted with ethyl acetate three times, and the combined organic layer was dried over anhydrous Na_2SO_4. After concentration under reduced pressure, silica gel column purification with hexane/ethyl acetate (3/1, v/v) afforded (*Z*)-*N*-(2-deuterio-1,2-diphenylvinyl)benzamide (**1a-Ph-d_1**; 77 mg, 0.26 mmol, 98% D) in 68% yield.

Typical Procedure for Synthesis of Indoles 2 under Conditions Catalytic in Copper. The synthesis of **2a** is representative (Scheme 2). $Cu(OPiv)_2$ (8.0 mg, 0.030 mmol), (*Z*)-*N*-(1,2-diphenylvinyl)picolinamide (**1a-Py**; 30 mg, 0.10 mmol), pivalic acid (15 mg, 0.15 mmol),

and MnO_2 (17 mg, 0.20 mmol) were placed in a microwave vessel. The vessel was flushed with nitrogen and then sealed with a cap. DMF (0.60 mL) was sequentially injected via a syringe. The mixture was irradiated under microwave reactor conditions at 200 °C for 1 h. The resulting mixture was then quenched with water, and a small amount of ethylenediamine was added to dissolve the residual copper salts in the aqueous phase. The mixture was extracted with ethyl acetate three times, and the combined organic layer was dried over anhydrous Na_2SO_4. After concentration under reduced pressure, silica gel column purification with hexane/ethyl acetate (10/1, v/v) afforded 2-phenylindole (**2a**; 18 mg, 0.091 mmol) in 91% yield.

2-Phenyl-1*H*-indole (**2a**)[19] white solid; m.p. 187.6-189.3 °C; 18 mg (91%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (dd, *J* = 1.1, 1.9 Hz, 1H), 7.15 (ddd, *J* = 1.1, 7.0, 8.0 Hz, 1H), 7.22 (ddd, *J* = 1.1, 7.1, 8.2 Hz, 1H), 7.34 (tt, *J* = 1.1, 7.4 Hz, 1H), 7.40-7.48 (m, 3H), 7.65-7.69 (m, 3H), 8.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.0, 110.9, 120.3, 120.7, 122.4, 125.2, 127.7, 129.1, 129.3, 132.4, 136.8, 137.9; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{14}H_{12}N$: 194.0964, found: 194.0960.

6-Methyl-2-(*p*-tolyl)-1*H*-indole (**2b**) white solid; m.p. 187.6-189.3 °C; 13 mg (59%); m.p. 206.8-208.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.47 (s, 3H), 6.73 (dd, *J* = 0.8, 2.1 Hz, 1H), 6.94 (dd, *J* = 0.8, 8.0 Hz, 1H), 7.18 (d, *J* = 0.6 Hz, 1H), 7.22-7.25 (m, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.50-7.55 (m, 2H), 8.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 21.8, 99.1, 110.8, 120.1, 122.0, 124.9, 127.1, 129.7, 129.8, 132.0, 137.1, 137.38, 137.40; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{16}N$: 222.1277, found: 222.1278.

6-(*tert*-Butyl)-2-(4-(*tert*-butyl)phenyl)-1*H*-indole (**2c**) white solid; m.p. 142.9-144.6 °C; 22 mg (71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 9H), 1.39 (s, 9H), 6.74 (t, *J* = 1.0 Hz, 1H), 7.20 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.40 (s, 1H), 7.44-7.47 (m, 2H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.57-7.59 (m, 2H), 8.23 (s,

1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 31.8, 34.7, 34.8, 99.2, 107.1, 118.5, 120.0, 124.8, 126.0, 127.0, 129.9, 136.9, 137.7, 145.7, 150.6; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{28}N$: 306.2216, found: 306.2218.

6-(Trifluoromethyl)-2-(4-(trifluoromethyl)phenyl)-1*H*-indole (**2d**) white solid; m.p. 115.9-116.8 ^{o}C; 30 mg (91%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (d, *J* = 1.4 Hz, 1H), 7.38 (dd, *J* = 1.0, 8.3 Hz, 1H), 7.69-7.77 (m, 6H), 8.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 101.6, 108.7 (q, *J* = 4.3 Hz), 117.3 (q, *J* = 3.7 Hz), 121.4, 124.0 (q, *J* = 273.8 Hz), 125.0 (q, *J* = 271.1 Hz), 125.1 (q, *J* = 31.7 Hz), 125.5, 126.2 (q, *J* = 3.4 Hz), 130.2 (q, *J* = 32.7 Hz), 131.3, 134.9, 135.9, 138.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.6, -60.8; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{10}F_6N$: 330.0712, found: 330.0709.

6-Chloro-2-(4-chlorophenyl)-1*H*-indole (**2e**) white solid; m.p. 166.2-167.2 ^{o}C; 19 mg (74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (dd, *J* = 0.8, 2.2 Hz, 1H), 7.10 (dd, *J* = 1.8, 8.4 Hz, 1H), 7.38 (t, *J* = 0.8 Hz, 1H), 7.38-7.43 (m, 2H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.55-7.58 (m, 2H), 8.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.4, 110.9, 121.3, 121.6, 126.3, 127.7, 128.4, 129.3, 130.4, 133.8, 137.2, 137.4; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{14}H_{10}Cl_2N$: 262.0185, found: 262.0184.

6-Bromo-2-(4-bromophenyl)-1*H*-indole (**2f**) white solid; m.p. 187.6-188.3 ^{o}C; 18 mg (51%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (d, *J* = 1.4 Hz, 1H), 7.23 (dd, *J* = 1.4, 8.4 Hz, 1H), 7.49 (t, *J* = 8.7 Hz, 3H), 7.54-7.58 (m, 3H), 8.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.5, 113.9, 116.0, 121.9, 123.9, 126.4, 126.6, 128.0, 130.8, 132.3, 137.3, 137.6; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{14}H_{10}Br_2N$: 349.9175, found: 349.9179.

2-(4-Methoxyphenyl)-1*H*-indole (**2g**) white solid; m.p. 228.5-229.7 ^{o}C; 14 mg (62%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 6.72 (dd, *J* = 0.8, 2.0 Hz, 1H), 6.96-7.00 (m, 2H), 7.09-7.19 (m, 2H),

7.37-7.39 (m, 1H), 7.58-7.61 (m, 3H), 8.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 98.9, 110.7, 114.5, 120.2, 120.4, 121.9, 125.2, 126.5, 129.4, 136.7, 138.0, 159.4; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{14}NO$: 224.1070, found: 224.1072.

5-Methyl-2-(*m*-tolyl)-1*H*-indole (2h) white solid; m.p. 160.9-161.6 °C; 19 mg (58%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.44 (s, 3H), 6.72 (dd, *J* = 0.6, 2.0 Hz, 1H), 7.00 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 7. 24-7.32 (m, 2H), 7.40 (d, *J* = 0.6 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.45 (s, 1H), 8.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 21.6, 99.4, 110.5, 120.3, 122.2, 123.9, 125.8, 128.4, 128.9, 129.4, 129.6, 132.4, 135.1, 138.1, 138.6; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{16}N$: 222.1277, found: 222.1275.

A 10:1 mixture of 5-methoxy-2-(3-methoxyphenyl)-1*H*-indole (**2i**) and **7-methoxy-2-(3-methoxyphenyl)-1*H*-indole** (**2i'**) white solid; m.p. 132.2-133.9 °C; 19 mg (75%); ^{1}H NMR (400 MHz, $CDCl_3$) for mixture δ 3.86 (s, 0.91 × 3H for **2i**), 3.87 (s, 0.91 × 3H for **2i**), 3.88 (s, 0.090 × 3H for **2i'**), 3.98 (s, 0.090 × 3H for **2i'**), 6.75 (dd, *J* = 0.7, 2.0 Hz, 0.91 × 1H for **2i**), 6.80 (d, *J* = 2.3 Hz, 0.090 × 1H for **2i'**), 6.84-6.88 (m, 0.91 × 2H for **2i**, 0.090 × 2H for **2i'**), 7.03 (t, *J* = 7.9 Hz, 0.090 × 1H for **2i'**), 7.07-7.08 (m, 0.91 × 1H for **2i**, 0.090 × 1H for **2i'**), 7.17 (t, *J* = 2.0 Hz, 0.91 × 1H for **2i**), 7.21-7.24 (m, 0.91 × 1H for **2i**, 0.090 × 1H for **2i'**), 7.26-7.28 (m, 0.91 × 1H for **2i**, 0.090 × 1H for **2i'**), 7.32-7.36 (m, 0.91 × 1H for **2i**, 0.090 × 1H for **2i'**), 8.23 (s, 0.91 × 1H for **2i**), 8.54 (s, 0.090 × 1H for **2i'**); ^{13}C NMR (100 MHz, $CDCl_3$) for **2i** δ 55.4, 55.8, 100.1, 102.2, 110.9, 111.7, 112.7, 113.0, 117.6, 129.6, 130.1, 132.0, 133.8, 138.5, 154.5, 160.1; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{16}NO_2$: 254.1176, found: 254.1174.

2-(Naphthalen-2-yl)-1*H*-benzo[*f*]indole (**2j**) white solid; m.p. 251.3-253.0 °C; 12 mg (40%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.25-7.35 (m, 3H), 7.54-7.62 (m, 2H), 7.90-8.05 (m, 6H), 8.13-8.15 (m,

2H), 8.52 (s, 1H), 11.73 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 99.2, 106.5, 117.5, 122.7, 123.7, 124.2, 124.5, 126.9, 127.3, 127.7, 128.2, 128.3, 128.5, 128.9, 129.0, 129.7, 130.6, 131.08, 131.14, 133.6, 138.6, 142.3; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{16}N$: 294.1277; found: 294.1275.

2-Butyl-1*H*-indole (**2m**) yellow oil; 13 mg (66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.3 Hz, 3H), 1.41 (sext, *J* = 7.5 Hz, 2H), 1.66-1.73 (m, 2H), 2.74 (t, *J* = 7.6 Hz, 2H), 6.23 (dd, *J* = 0.9, 2.0 Hz, 1H), 7.04-7.12 (m, 2H), 7.27-7.29 (m, 1H), 7.51-7.53 (m, 1H), 7.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.4, 28.0, 31.3, 99.5, 110.3, 119.6, 119.7, 120.9, 128.9, 135.8, 140.0; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{12}H_{16}N$: 174.1277, found: 174.1275.

2-Cyclohexyl-1*H*-indole (**2n**) white solid; m.p. 104.2-105.6 ^{o}C; 16 mg (79%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23-1.51 (m, 5H), 1.74-1.77 (m, 1H), 1.83-1,87 (m, 2H), 2.07-2.10 (m, 2H), 2.68-2.75 (m, 1H), 6.23 (d, *J* = 1.0 Hz, 1H), 7.04-7.13 (m, 2H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 26.3, 33.0, 37.3, 97.5, 110.3, 119.6, 119.9, 120.9, 128.6, 135.5, 145.1; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{14}H_{18}N$: 200.1434, found: 200.1434.

Typical Procedure for Synthesis of Indoles 2 under Conditions Stoichiometric in Copper. The synthesis of **2k** is representative (Scheme 2). $Cu(OPiv)_2$ (53 mg, 0.20 mmol), (*Z*)-*N*-(1,2-di(thiophen-2-yl)vinyl)picolinamide (**1k-Py**; 31 mg, 0.10 mmol), and pivalic acid (15 mg, 0.15 mmol) were placed in a 2.0 mL microwave vessel. The vessel was flushed with nitrogen and then sealed with a cap. DMF (0.60 mL) was sequentially injected via a syringe. The mixture was heated at 150 °C for 4 h with an oil bath. The resulting mixture was then quenched with water, and a small amount of ethylenediamine was added to dissolve the residual copper salts in the aqueous phase. The mixture was extracted with ethyl acetate three times, and the combined organic layer was dried over anhydrous Na_2SO_4. After concentration under reduced pressure, silica gel column purification with

hexane/ethyl acetate (10/1, v/v) afforded 5-(thiophen-2-yl)-4*H*-thieno[3,2-*b*]pyrrole (**2k**; 8.2 mg, 0.41 mmol) in 41% yield.

5-(Thiophen-2-yl)-4*H*-thieno[3,2-*b*]pyrrole (**2k**) white solid; m.p. 110.6-111.9 ^{o}C; 8.4 mg (41%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (d, *J* = 1.8 Hz, 1H), 6.95 (dd, *J* = 0.6, 5.2 Hz, 1H), 7.05 (dd, *J* = 3.6, 5.0 Hz, 1H), 7.09 (d, *J* = 5.2 Hz, 1H), 7.12 (dd, *J* = 1.1, 3.6 Hz, 1H), 7.20 (dd, *J* = 1.1, 5.1 Hz, 1H), 8.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.7, 110.9, 121.6, 123.4, 124.2, 125.5, 127.8, 131.6, 136.1, 139.0; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{10}H_8NS_2$: 206.0093, found: 206.0095.

2-(Benzo[*b*]thiophen-2-yl)-1*H*-benzo[4,5]thieno[3,2-*b*]pyrrole (**2l**) brown solid; m.p. 196.2-197.5 ^{o}C; 5.8 mg (19%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (d, *J* = 1.9 Hz, 1H), 7.26-7.40 (m, 5H), 7.74-7.82 (m, 4H), 8.84 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.1, 117.4, 118.4, 122.2, 123.3, 123.4, 124.2, 124.30, 124.33, 124.6, 124.8, 126.4, 131.5, 133.6, 135.4, 138.5, 140.4, 142.3; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{12}NS_2$: 306.0406, found: 306.0394.

Typical Procedure for Synthesis of Oxazoles 3. The synthesis of **3a-Ph** is representative (Scheme 3). $Cu(OPiv)_2$ (8.0 mg, 0.030 mmol), (*Z*)-*N*-(1,2-diphenylvinyl)benzamide (**1a-Ph**; 30 mg, 0.10 mmol), pivalic acid (15 mg, 0.15 mmol), and MnO_2 (17 mg, 0.2 mmol) were placed in a microwave vessel. The vessel was flushed with nitrogen and then sealed with a cap. DMF (0.60 mL) was sequentially injected via a syringe. The mixture was irradiated under microwave reactor conditions at 200 °C for 1 h. The resulting mixture was then quenched with water, and a small amount of ethylenediamine was added to dissolve the residual copper salts in the aqueous phase. The mixture was extracted with ethyl acetate three times, and the combined organic layer was dried over anhydrous Na_2SO_4. After concentration under reduced pressure, silica gel column purification with hexane/ethyl acetate (20/1, v/v) afforded 2,4,5-triphenyloxazole (**3a-Ph**; 27 mg, 0.089 mmol) in 89% yield.

2,4,5-Triphenyloxazole (**3a-Ph**)[20] white solid; m.p. 112.9-113.5 °C; 260 mg (86%); 27 mg (89%) on a 0.10 mmol scale; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.42 (m, 6H), 7.45-7.51 (m, 3H), 7.66-7.69 (m, 2H), 7.71-7.74 (m, 2H), 8.15-8.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.5, 126.6, 127.4, 128.2, 128.3, 128.57, 128.65, 128.7, 128.8, 129.0, 130.4, 132.6, 136.8, 145.6, 160.2; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{16}NO$: 298.1226, found: 298.1228.

2-(4-Methoxyphenyl)-4,5-diphenyloxazole (**3a-OMe**) white solid; m.p. 110.9-111.9 °C; 29 mg (87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 6.98-7.00 (m, 2H), 7.32-7.42 (m, 6H), 7.65-7.67 (m, 2H), 7.71-7.73 (m, 2H), 8.07-8.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 114.2, 120.2, 126.5, 128.1, 128.17, 128.19, 128.4, 128.6, 128.7, 129.2, 132.7, 136.6, 145.0, 160.3, 161.4; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{18}NO_2$: 328.1332, found: 328.1331.

4,5-Diphenyl-2-(4-(trifluoromethyl)phenyl)oxazole (**3a-CF_3**) white solid; m.p. 137.8-139.9 °C; 33 mg (89%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.44 (m, 6H), 7.66-7.75 (m, 6H), 8.30 (d, J = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 123.9 (q, J = 272.4 Hz), 125.8 (q, J = 3.9 Hz), 126.6, 126.7, 128.1, 128.5, 128.6, 128.7, 128.8, 128.9, 130.5, 131.9 (q, J = 32.7 Hz), 132.2, 137.2, 146.4, 158.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.8; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{15}F_3NO$: 366.1100, found: 366.1104.

2-(*tert*-Butyl)-4,5-diphenyloxazole (**3a-*t*-Bu**) white solid; m.p. 58.9-60.3 °C; 24 mg (85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 7.27-7.38 (m, 6H), 7.56-7.59 (m, 2H), 7.63-7.66 (m, 2H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 28.7, 33.8, 126.3, 127.9, 128.1, 128.2, 128.55, 128.59, 129.4, 132.9, 134.9, 144.7, 169.9; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{19}H_{20}NO$: 278.1539, found: 278.1537.

2-Phenyl-4,5-di-*p*-tolyloxazole (**3b-Ph**) white solid; m.p. 131.3-132.0 °C; 30 mg (93%); ^1H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.39 (s, 3H), 7.18-7.22 (m, 4H), 7.44-7.50 (m, 3H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 8.13-8.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.38, 21.42, 126.3, 126.4, 126.5, 127.5, 128.0, 128.7, 129.3, 129.4, 129.8, 130.2, 136.3, 137.9, 138.5, 145.5, 159.8; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{20}NO$: 326.1539, found: 326.1538.

4,5-Bis(4-(*tert*-butyl)phenyl)-2-phenyloxazole (**3c-Ph**) white solid; m.p. 154.2-155.6 °C; 37 mg (89%); ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 9H), 1.36 (s, 9H), 7.41-7.49 (m, 7H), 7.65-7.70 (m, 4H), 8.13-8.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.25, 31.34, 34.7, 34.8, 125.5, 125.6, 126.2, 126.3, 126.4, 127.6, 127.7, 128.7, 129.8, 130.2, 136.3, 145.4, 151.1, 151.6, 159.8; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{29}H_{32}NO$: 410.2478, found: 410.2474.

2-Phenyl-4,5-bis(4-(trifluoromethyl)phenyl)oxazole (**3d-Ph**) white solid; m.p. 165.3-166.0 °C; 40 mg (92%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50-7.53 (m, 3H), 7.66-7.70 (m, 4H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 8.13-8.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 123.8 (q, *J* = 270.5 Hz), 124.0 (q, *J* = 270.5 Hz), 125.8 (q, *J* = 3.6 Hz), 125.9 (q, *J* = 3.9 Hz), 126.66, 126.74, 128.4, 128.9, 130.0, 130.6 (q, *J* = 33.0 Hz), 130.7 (q, *J* = 32.3 Hz), 131.87, 131.89, 135.7, 137.0, 144.9, 161.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8, −62.7; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{14}F_6NO$: 434.0974, found: 434.0976.

4,5-Bis(4-chlorophenyl)-2-phenyloxazole (**3e-Ph**) white solid; m.p. 145.9-147.0 ^{o}C; 29 mg (78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.40 (m, 4H), 7.47-7.50 (m, 3H), 7.57-7.59 (m, 2H), 7.63-7.66 (m, 2H), 8.11-8.14 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 126.5, 127.0, 127.2, 127.8, 128.9, 129.0, 129.1, 129.4, 130.7, 130.8, 134.3, 134.7, 136.1, 144.7, 160.5; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{14}Cl_2NO$: 366.0447, found: 366.0446.

4,5-Bis(4-bromophenyl)-2-phenyloxazole (**3f-Ph**) white solid; m.p. 165.9-167.9 ^{o}C; 17 mg (53%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.60 (m, 11H), 8.12-8.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$)) δ 122.5, 122.9, 126.5, 127.0, 127.6, 128.0, 128.9, 129.6, 130.70, 130.71, 131.2, 132.0, 132.1, 136.2, 160.6; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{14}Br_2NO$: 453.9437, found: 453.9423.

4-(4-Methoxyphenyl)-2,5-diphenyloxazole (**3g-Ph**) white solid; m.p. 127.2-127.9 ^{o}C; 31 mg (93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.93-6.96 (m, 2H), 7.30-7.41 (m, 3H), 7.45-7.51 (m, 3H), 7.63-7.69 (m, 4H), 8.13-8.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 114.1, 125.0, 126.39, 126.44, 127.5, 128.4, 128.7, 128.8, 129.2, 129.5, 130.3, 136.6, 144.9, 159.6, 160.0; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{18}NO_2$: 328.1132, found: 328.1131.

2-Phenyl-4,5-di-*m*-tolyloxazole (**3h-Ph**) colorless liquid; 29 mg (90%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.38 (s, 3H), 7.14-7.18 (m, 2H), 7.23-7.29 (m, 2H), 7.45-7.50 (m, 5H), 7.53 (s, 1H), 7.60 (s, 1H), 8.14-8.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.47, 21.49, 123.8, 125.2, 126.5, 127.1, 127.5, 128.4, 128.6, 128.77, 128.82, 129.96, 129.99, 129.3, 130.3, 132.5, 136.8, 138.3, 138.4, 145.7, 160.0; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{20}NO$; 326.1539, found: 326.1537.

4,5-Bis(3-methoxyphenyl)-2-phenyloxazole (**3i-Ph**) white solid; m.p. 73.9-75.2 ^{o}C; 34 mg (96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.82 (s, 3H), 6.88-6.93 (m, 2H), 7.23-7.24 (m, 1H), 7.27-7.33 (m, 5H), 7.46-7.51 (m, 3H), 8.15-8.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.29, 55.33, 111.8, 113.3, 114.6, 119.1, 120.7, 126.5, 127.3, 128.8, 129.6, 129.8, 130.1, 130.41, 130.43, 133.8, 136.9, 145.5, 159.7, 159.8, 160.0; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{20}NO_3$: 358.1438, found: 358.1436.

4,5-Di(naphthalen-2-yl)-2-phenyloxazole (**3j-Ph**) white solid; m.p. 180.3-181.3 ^{o}C; 37 mg (94%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.55 (m, 7H), 7.75 (dd, *J* = 1.7, 8.6 Hz, 1H), 7.80-7.88 (m, 7H), 8.23-8.26 (m, 3H), 8.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.2, 125.89, 125.92, 126.31, 126.34, 126.4, 126.6, 126.68, 126.74, 127.4, 127.7, 127.8, 128.2, 128.36, 128.38, 128.39, 128.85, 128.88, 130.0, 130.5, 133.17, 133.21, 133.3, 133.5, 137.2, 146.0, 160.5; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{29}H_{20}NO$: 398.1539, found: 398.1537.

2-Phenyl-4,5-di(thiophen-2-yl)oxazole (**3k-Ph**) white solid; m.p. 102.9-104.2 ^{o}C; 28 mg (89%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (dd, *J* = 3.6, 5.2 Hz, 1H), 7.13 (dd, *J* = 3.6, 5.1 H, 1H), 7.39 (dd, *J* = 1.0, 5.1 Hz, 1H), 7.42 (dd, *J* = 1.0, 5.1 Hz, 1H), 7.47-7.52 (m, 3H), 7.55-7.56 (m, 2H), 8.11-8.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.26, 126.31, 126.6, 126.76, 126.83, 126.9, 127.5, 127.6, 128.8, 129.7, 130.7, 131.4, 134.0, 140.4, 159.9; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{17}H_{12}NOS_2$: 310.0355, found: 310.0356.

4,5-Bis(benzo[*b*]thiophen-2-yl)-2-phenyloxazole (**3l-Ph**) white solid; m.p. 236.9-238.6 ^{o}C; 39 mg (96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.54 (m, 4H), 7.50-7.54 (m, 3H), 7.82-7.91 (m, 6H),

8.18-8.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 122.26, 122.29, 123.4, 123.6, 123.9, 124.1, 124.6, 124.86, 124.92, 125.4, 126.6, 126.8, 128.9, 129.3, 131.0, 132.8, 133.9, 139.4, 139.8, 140.0, 140.2, 141.4, 160.6; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{25}H_{16}NOS_2$: 410.0668, found: 410.0677.

4-Butyl-2,5-diphenyloxazole (**3m-Ph**) colorless liquid; 14 mg (49%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.3 Hz, 3H), 1.47 (sext, *J* = 7.5 Hz, 2H), 1.74-1.82 (m, 2H), 2.82 (t, *J* = 7.9 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.42-7.49 (m, 5H), 7.67-7.69 (m, 2H), 8.08-8.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.7, 27.1, 31.1, 125.5, 126.3, 127.6, 127.7, 128.7, 128.8, 129.3, 130.1, 138.2, 145.2, 159.5; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{19}H_{20}NO$: 278.1539, found: 278.1540.

4-Cyclohexyl-2,5-diphenyloxazole (**3n-Ph**) white solid; m.p. 133.6-134.0 ^{o}C; 24 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38-1.42 (m, 3H), 1.75-1.89 (m, 7H), 2.86-2.93 (m, 1H), 7.34 (tt, *J* = 1.2, 7.4 Hz, 1H), 7.42-7.49 (m, 5H), 7.63-7.66 (m, 2H), 8.07-8.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 26.5, 31.0, 36.0, 126.0, 126.4, 127.7, 127.8, 128.7, 128.8, 129.4, 129.9, 142.8, 144.3, 159.7; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{22}NO$: 304.1696, found: 304.1697.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publication website at DOI: 10.1021/acs.joc.7b00682.

^{1}H, ^{13}C{^{1}H}, and ^{19}F{^{1}H} NMR spectra for products and kinetic profiles (PDF)

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Notes

The authors declare no competing financial interest.

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