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Room Temperature Copper(II)-Catalyzed Oxidative Cyclization of Enamides to 2,5-Disubstituted Oxazoles via Vinylic C−H Functionalization

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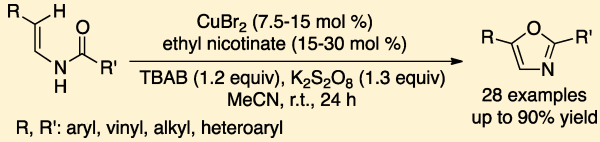
Supporting Information

ABSTRACT: A copper(II)-catalyzed oxidative cyclization of enamides to oxazoles via vinylic C−H bond functionalization at room temperature is described. Various 2,5-disubstituted oxazoles bearing aryl, vinyl, alkyl, and heteroaryl substituents could be synthesized in moderate to high yields. This reaction protocol is complementary to our previously reported iodine-mediated cyclization of enamides to afford 2,4,5-trisubstituted oxazoles.



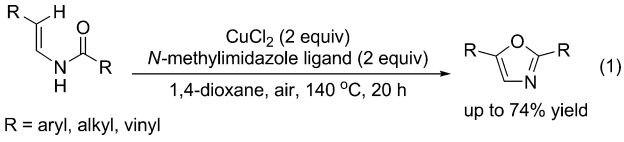
INTRODUCTION

Substituted oxazoles can be found in a wide variety of biologically active molecules of interest to the drug discovery community. Oxazole-containing biologically active natural products,[1] especially the diazonamide[1b] and phorboxazole[1c] families, exhibit anticancer properties, and a number of synthetic trisubstituted[2] and 2,5-disubstituted[3] oxazoles have been evaluated to show activity against diabetes,[2b] Gram-positive and Gram-negative bacterial infections,[3a] breast cancer,[3b] and pancreatic cancer[3c] (Figure 1). Moreover, substituted oxazoles can be utilized in agrochemicals,[4] fluorescent dyes,[5] and polymers[6] and also as ligands for transition-metal catalysis.[7] Consequently, the development of synthetic methods to access functionalized oxazoles is of great importance to synthetic organic chemists.

To date, various synthetic methods have been developed for the synthesis of substituted oxazoles.[8−10] In particular, a common strategy has been to convert an acyclic precursor to an oxazole ring.[8a−d,i,9,10] A versatile cyclization strategy is the Robinson−Gabriel condensation,[8a−d] which has been utilized to prepare a range of highly substituted and complex oxazoles (Scheme 1A). However, this method requires the use of Brönsted acid catalysts or Lewis acid reagents, which limits the overall functional group tolerance of the transformation. Alternatively, enamides can serve as stable and easily accessible starting materials to afford oxazoles.[9,10] Enamides bearing the β-vinylic C—heteroatom bonds (C−Br,[9a−d] C−I,[9e,f] and C−S[9g]) have been isolated or generated *in situ*, which undergo facile intramolecular vinylation of the amide oxygen to provide a broader range of oxazoles under milder conditions (Scheme 1B). While this strategy is effective, a method for the cyclization of enamides to oxazoles, without the need for further vinylic C−H functionalization, would be a more direct and convenient means of obtaining the same products (Scheme 1C).

Our group previously reported the development of a sequential synthesis of 2,4,5-trisubstituted oxazoles via initial copper-catalyzed amidation of vinyl halides to form enamides, followed by intramolecular cyclization promoted by iodine (Scheme 2).[10] Unfortunately, the synthesis of mono- and disubstituted oxazoles still remained a limitation under the reported reaction conditions, and 2,5-disubstituted oxazoles were instead generated via a domino copper-catalyzed C−N/C−O coupling sequence starting from 1,2-dihaloalkenes and amides. Thus, the development of a direct cyclization of enamides to oxazoles without the need for a β-vinylic functional group remains an important challenge.

Recently, several examples of transition-metal-catalyzed methods for the direct vinylic C−H functionalization of enamides have been described.[11] Moreover, copper, as an inexpensive and readily available metal, has been widely utilized to facilitate C−O bond formation, via oxidative C−H functionalization, for the formation of various heterocycles.[12] We thus reasoned that a Cu-catalyzed direct oxidative cyclization of enamides to oxazoles via vinylic C−H functionalization might be plausible. In fact, during the preparation of this manuscript, Wendlandt and Stahl disclosed a similar method for the Cu-mediated oxidative cyclization of enamides to 2,5-disubstituted oxazoles (eq 1).[13] Their method



is attractive as it uses oxygen as the oxidant, albeit with a stoichiometric quantity of copper(II) chloride, to promote this cyclization. Herein, we report a method for the synthesis of a broad range of 2,5-disubstituted oxazoles via stepwise Cu-

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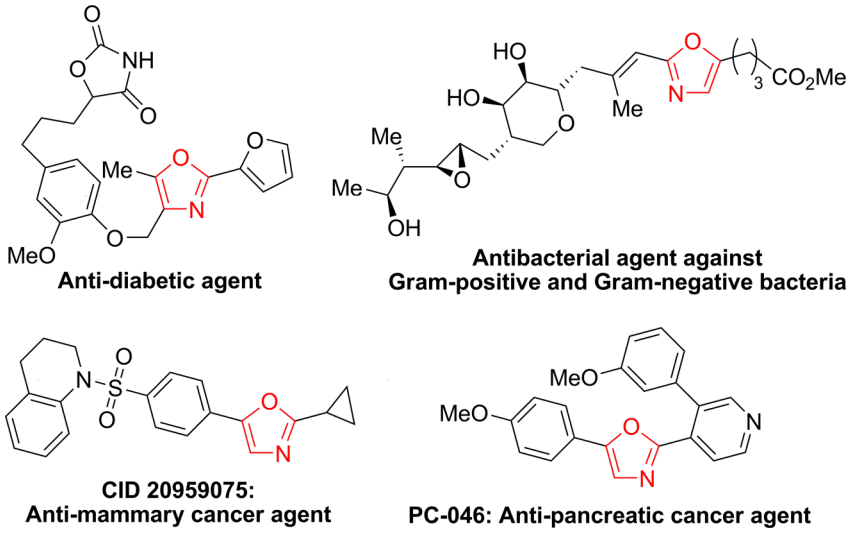
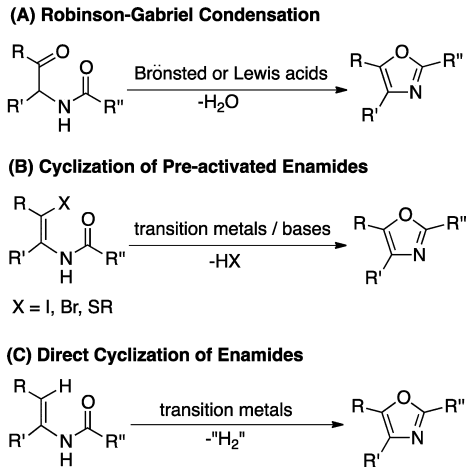


Figure 1. Selected biologically active oxazoles.

Scheme 1. Approaches to Oxazole Synthesis via Cyclization



catalyzed amidation of vinyl halides to form enamides, followed by subsequent Cu-catalyzed oxidative cyclization, promoted by potassium persulfate, of the enamide intermediates under ambient conditions (Scheme 3).

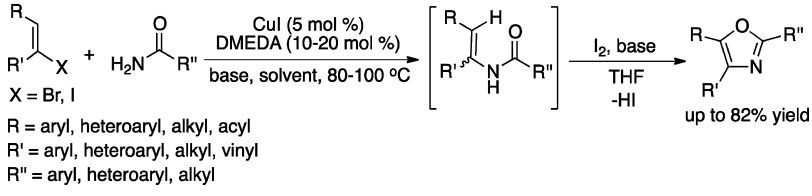
RESULTS AND DISCUSSION

We began our studies by subjecting (*E*)-*N*-styrylbenzamide (**1a**) to a catalytic amount of copper(II) bromide, using potassium persulfate as an oxidant (Table 1, entry 1). Despite complete conversion of **1a**, 2,5-diphenyloxazole (**2a**) was obtained in only 14% yield.[14] The use of tetrabutylammonium bromide (TBAB) as an additive,[15] which probably aids in the regeneration of $CuBr_2$, led to a significant increase in yield (59%, Table 1, entry 2). Further, we found that the use of ethyl nicotinate (40 mol %) as a ligand for copper increased the yield up to 78% (Table 1, entry 3). A number of electronically varied substituted pyridine ligands were evaluated (Table 1, entries 3–7), and ethyl nicotinate was identified as the optimal ligand. In an attempt to reduce the loading of ethyl nicotinate, we found that by slightly increasing the amount of copper catalyst to 7.5 mol %, the amount of ethyl nicotinate could be lowered to 15 mol % while maintaining a high yield of product (Table 1, entry 9). The use of $CuBr_2$ was also found to be much more effective than the other transition metal salts ($CuCl_2$, $FeBr_2$, and $FeCl_2$) (Table 1, entries 11–13).[16] In the absence of $CuBr_2$, only a trace of **2a** was obtained (Table 1, entry 14).

With good reaction conditions, we set out to examine the substrate scope for the process (Table 2). The process tolerates a range of *ortho*-, *meta*-, and *para*-substituents on either or both aromatic rings of the enamide intermediate to generally afford 2,5-diaryloxazoles in good yields. Notably, chloro- and bromo-substituted diaryloxazoles (**2d**, **2l**, and **2m**) could be prepared, which render them as suitable substrates for further functionalization via a range of cross-coupling methods. Moreover, these conditions described also provide access to 2,5-diaryloxazoles bearing fluoro and trifluoromethyl substituents (**2e**, **2f**, **2n**, and **2o**), which are often highly desirable in the synthesis of novel therapeutics.[17] *Ortho*-substitution on the enamide aryl groups was also well-tolerated, affording the corresponding oxazoles in high yields (**2p**, **2q**). The presence of a highly electron-withdrawing nitro group on the benzamide region (**2g**, **2h**) or of a strongly π-donating methoxy group on the β-styryl region (**2i**)[18] led to lower yields of the corresponding oxazoles.

Next, we sought to extend this methodology to include 2,5-disubstituted oxazoles bearing vinyl, alkyl, and heterocyclic

Scheme 2. Sequential Synthesis of Trisubstituted Oxazoles via Coupling and Cyclization



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Scheme 3. Improved Cu-Catalyzed Oxidative Cyclization of Enamides to 2,5-Disubstituted Oxazoles

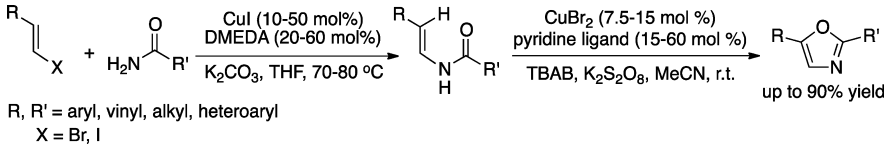
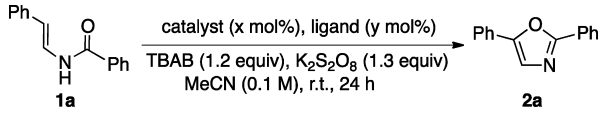


Table 1. Optimization of Oxidative Cyclization of Enamide[a]



entry	catalyst (x mol %)	ligand (y mol %)	conversion (%)[b]	% yield of **2a**[c]
1[d]	$CuBr_2$ (5)	none	100	14[e]
2	$CuBr_2$ (5)	none	100	59
3	$CuBr_2$ (5)	ethyl nicotinate (40)	100	78
4	$CuBr_2$ (5)	3-nitropyridine (40)	100	62
5	$CuBr_2$ (5)	3-cyanopyridine (40)	100	59
6	$CuBr_2$ (5)	2-fluoropyridine (40)	100	64
7	$CuBr_2$ (5)	pyridine (40)	100	54
8	$CuBr_2$ (5)	ethyl nicotinate (10)	100	66
9	$CuBr_2$ (7.5)	ethyl nicotinate (15)	100	84
10	$CuBr_2$ (10)	ethyl nicotinate (20)	100	80
11	$CuCl_2$ (5)[f]	ethyl nicotinate (10)	39	2[e]
12	$FeBr_2$ (20)	ethyl nicotinate (40)	75	24[e]
13	$FeCl_2$ (20)[f]	ethyl nicotinate (40)	49	0
14	none	ethyl nicotinate (15)	50	2[e]

[a]Reaction conditions: enamide (0.2 mmol), tetrabutylammonium bromide (TBAB) (0.24 mmol), $K_2S_2O_8$ (0.26 mmol), $CuBr_2$ (x mol %), ligand (y mol %), acetonitrile (2 mL), rt, 24 h, argon atmosphere. [b]Determined by GC. [c]Isolated yield. [d]No TBAB was added. [e]GC yield using n-dodecane as an internal standard. [f]Tetrabutylammonium chloride (TBAC) (1.2 equiv) was used.

substitution (Table 3). Enamides bearing the styryl groups could be cyclized to afford the styryloxazoles (**4a**,**b**), including the natural product annuloline (**4c**).[19] Enamides bearing both cyclic and acyclic alkyl groups were also viable substrates (**4d**–**f**), although, interestingly, the cyclohexyl ring of oxazole **4f** was partially oxidized to 1-cyclohexenyl (**4f′**) during the course of the reaction. We were particularly pleased to discover that enamides bearing electron-rich 2-furyl, 2- and 3-thienyl, and *N*-benzoyl-5-indolyl groups survived the oxidizing conditions to afford the corresponding oxazoles in moderate to high yields (**4g**–**k**). Unfortunately, an oxazole containing an *N*-methyl-2-pyrrolyl group at the 2-position, as well as oxazoles bearing *N*-tosyl-2-pyrrolyl and 2-thienyl groups at the 5-position, could not be efficiently synthesized using the current conditions. Moreover, oxazoles with pyridyl groups, as well as an oxazole bearing a *N*-methyl-2-imidazolyl group at the 2-position, could be generated only in low yields.

Regarding the mechanism of copper(II)-catalyzed oxidative cyclization of enamides to oxazoles, Wendlandt and Stahl have proposed that $CuCl_2$ acts as a single-electron oxidant, triggering the cyclization via a radical pathway (eq 1).[13] We concur; in our case, $CuBr_2$ most likely serves as a single-electron oxidant, converting the electron-rich enamide **1a** to an enamide radical cation (Scheme 4, transformation i), which then cyclizes to radical intermediate **I** (Scheme 4, transformation ii).[13] Subsequent oxidation of **I** by $CuBr_2$ provides the oxazole **2a** (Scheme 4, transformation iii). The reduced form of copper, CuBr, is then oxidized by $K_2S_2O_8$ and reacts with TBAB to regenerate the $CuBr_2$ catalyst (Scheme 4, transformation iv).

CONCLUSION

In summary, we have developed an efficient room temperature catalytic oxidative cyclization of enamides to generate 2,5-disubstituted oxazoles by using catalytic amounts of $CuBr_2$ in conjunction with $K_2S_2O_8$ as an oxidant. This reaction protocol can tolerate enamide substrates bearing aryl, heteroaryl, vinyl, and/or alkyl substituents to afford the corresponding oxazoles in moderate to high yields. This transformation is complementary to the iodine-promoted cyclization of enamides to 2,4,5-trisubstituted oxazoles previously reported by our group.

EXPERIMENTAL SECTION

General Information. Nuclear magnetic resonance spectra were recorded on a Bruker 400 MHz instrument at ambient temperature. All ^{1}H NMR spectra were measured in parts per million (ppm) relative to the signals for tetramethylsilane (TMS) added into the deuterated chloroform ($CDCl_3$) (0 ppm) or the signals for residual dimethyl sulfoxide (DMSO) in deuterated DMSO (DMSO-d_6) (2.50 ppm). Data for ^{1}H NMR were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, m = multiplet, br = broad, ovrlp = overlap), coupling constants, and integration. All ^{13}C NMR spectra were reported in ppm relative to $CDCl_3$ (77.16 ppm)[20] or DMSO-d_6 (25.12 ppm).[20] All ^{19}F NMR spectra were reported in ppm relative to a $CFCl_3$ external standard (0 ppm). Anhydrous acetonitrile (99.8%) was purchased from Alfa Aesar. Other commercial materials were used as received unless otherwise noted. Flash column chromatography was performed using Silicycle silica gel (ultra pure grade). (*E*)-(2-bromovinyl)benzene,[21] (*E*)-1-(2-bromovinyl)-4-methoxybenzene,[21] (*E*)-1-(2-bromovinyl)-4-methylbenzene,[21] (*E*)-1-(2-bromovinyl)-4-chlorobenzene,[21] (*E*)-1-iododec-1-ene,[22] ((1*E*)-4-bromobuta-1,3-dien-1-yl)benzene[23] ((3*Z*):(3*E*) = 2.6:1.0), and (*E*)-3-(3,4-dimethoxyphenyl)acrylamide[24] were prepared according to the literature procedures.

General Procedure for the Preparation of β-Aryl-vinyl Bromides. Adapted from a previously reported procedure with some modification.[21] A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stir bar was charged with the cinnamic acid or its derivatives (1.0 equiv), *N*-bromosuccinimide (NBS) (1.05 equiv), and manganese(II) acetate tetrahydrate ($Mn(OAc)_2{\cdot}4H_2O$) (20 mol %), followed by acetonitrile and water (1:1). The reaction mixture was stirred overnight at room temperature. The reaction mixture was then washed with excess water and ethyl acetate in a separation funnel. The aqueous fraction was further washed with ethyl acetate until most of the product has been extracted as judged by TLC analysis. The combined organic fraction was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (ethyl acetate (EtOAc)/hexanes = 1: 20) to afford the desired vinyl bromide. The ratio of (*E*):(*Z*) isomers of vinyl bromide was determined by ^{1}H NMR spectroscopy.

(*E*)-4-(2-Bromovinyl)phenyl Acetate (S1)[25] ((*E*):(*Z*) > 99:1). Synthesized from *trans*-4-acetoxycinnamic acid (4.50 g, 21.8 mmol), $Mn(OAc)_2{\cdot}4H_2O$ (1.07 g, 4.36 mmol), and NBS (4.07 g, 22.9 mmol) in acetonitrile/water (50 mL/50 mL); 3.23 g, 13.4 mmol, 61%; off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 2H), 7.10–7.04 (ovrlp, 3H), 6.73 (d, J = 14.0 Hz, 1H), 2.30 (s, 3H).

(*E*)-1-Bromo-4-(2-bromovinyl)benzene (S2)[26] ((*E*):(*Z*) > 99:1). Synthesized from *trans*-4-bromocinnamic acid (13.4 g, 59.0 mmol),

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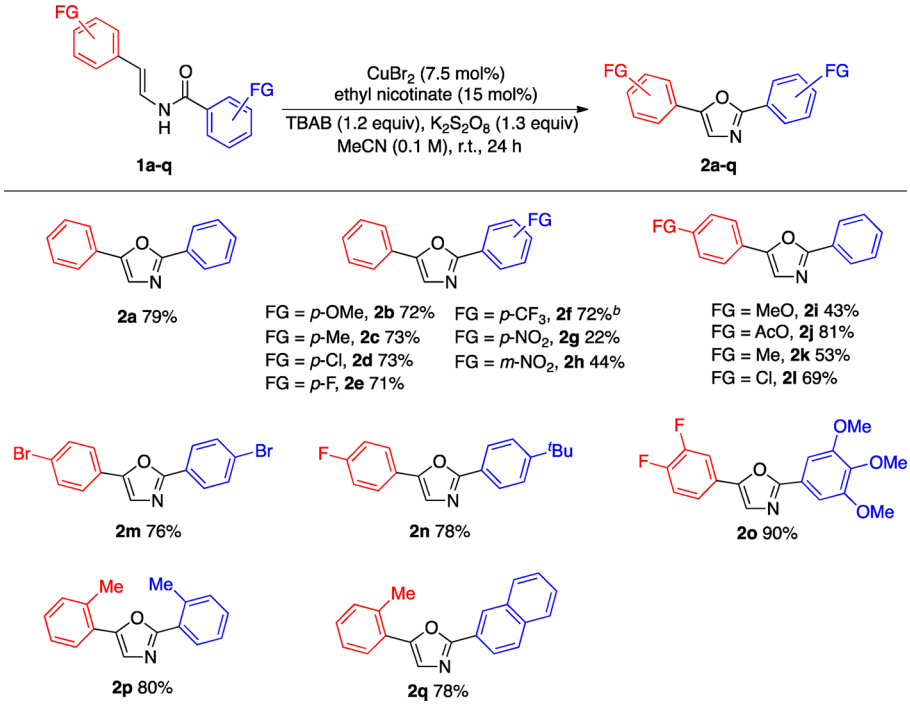
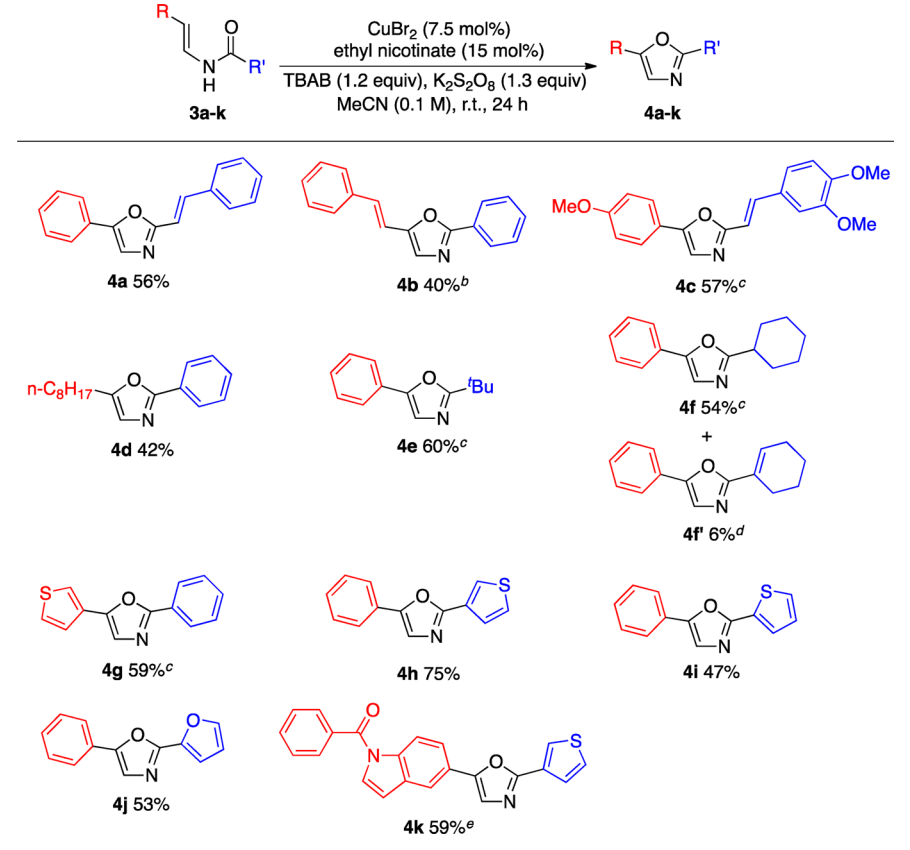
Table 2. Scope of Enamides bearing Aryl Groups[a]



[a]Reaction conditions: enamide (1 mmol), $CuBr_2$ (7.5 mol %), ethyl nicotinate (15 mol %), TBAB (1.2 mmol), $K_2S_2O_8$ (1.3 mmol), acetonitrile (10 mL), rt, 24 h, argon atmosphere; isolated yields based on an average of two runs. [b]Enamide (0.8 mmol).

Table 3. Scope of Enamides Bearing Vinyl, Alkyl, and Heteroaryl Groups[a]



[a]Reaction conditions: enamide (1 mmol), $CuBr_2$ (7.5 mol %), ethyl nicotinate (15 mol %), TBAB (1.2 mmol), $K_2S_2O_8$ (1.3 mmol), acetonitrile (10 mL), rt, 24 h, argon atmosphere; isolated yields based on an average of two runs. [b]$CuBr_2$ (15 mol %), pyridine (60 mol %). [c]$CuBr_2$ (15 mol %), ethyl nicotinate (30 mol %). [d]An inseparable dehydrogenated co-product was isolated; ratio of **4f**:**4f'** was determined by ^1H NMR spectroscopy. [e]Enamide (0.5 mmol).

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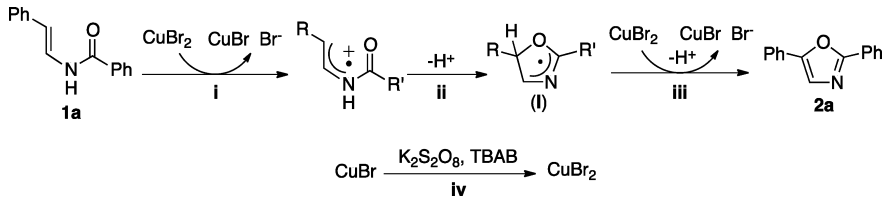
Scheme 4. Proposed Mechanism for Cu(II)-Catalyzed Oxidative Cyclization of 1a to 2a



$Mn(OAc)_2·4H_2O$ (2.89 g, 11.8 mmol), and NBS (11.0 g, 62.0 mmol) in acetonitrile/water (100 mL/100 mL); 6.07 g, 23.2 mmol, 39%; off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 14.0 Hz, 1H), 6.78 (d, J = 14.0 Hz, 1H).

(*E*)-1-(2-Bromovinyl)-4-fluorobenzene (S3)[27] ((*E*):(*Z*) > 99:1). Synthesized from *trans*-4-fluorocinnamic acid (12.0 g, 72.2 mmol), $Mn(OAc)_2·4H_2O$ (3.54 g, 14.4 mmol), and NBS (13.5 g, 75.8 mmol) in acetonitrile/water (100 mL/100 mL); 7.31 g, 36.4 mmol, 50%; off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HF}$ = 5.6 Hz, 2H), 7.08 (d, J = 14.0 Hz, 1H), 7.04 (dd, $^3J_{HH}$ = 8.4 Hz, $^3J_{HF}$ = 8.4 Hz, 2H), 6.71 (d, J = 14.0 Hz, 1H).

(*E*)-4-(2-Bromovinyl)-1,2-difluorobenzene (S4)[28] ((*E*):(*Z*) ≈ 95:5). Synthesized from *trans*-3,4-difluorocinnamic acid (10.0 g, 54.3 mmol), $Mn(OAc)_2·4H_2O$ (2.66 g, 10.9 mmol), and NBS (10.2 g, 57.0 mmol); 2.45 g, 11.2 mmol, 21%; pale-yellow oil. ^{1}H NMR of (*E*)-isomer (400 MHz, $CDCl_3$) δ 7.14−7.08 (ovrlp, 2H), 7.02−6.99 (ovrlp, 2H), 6.72 (d, J = 14.4 Hz, 1H).

(*E*)-1-(2-Bromovinyl)-2-methylbenzene (S5)[29] ((*E*):(*Z*) > 99:1). Synthesized from *trans*-2-methylcinnamic acid (4.00 g, 24.7 mmol), $Mn(OAc)_2·4H_2O$ (1.21 g, 4.94 mmol), and NBS (4.62 g, 25.9 mmol) in acetonitrile/water (80 mL/80 mL); 2.64 g, 13.4 mmol, 54%; pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.27 (ovrlp, 2H), 7.21−7.12 (ovrlp, 3H), 6.60 (d, J = 14.0 Hz, 1H), 2.30 (s, 3H).

General Procedure for the Preparation of *β*-Heteroaryl-vinyl Bromides. Adapted from a previously reported procedure.[23] A 250 mL round-bottom flask was charged with a Teflon-coated magnetic stir bar, (bromomethyl)triphenylphosphonium bromide[30] (1.0 equiv), and potassium *tert*-butoxide (KO^tBu) (1.05 equiv). The reaction vessel was evacuated and backfilled with argon (this sequence was repeated a total of 3 times) and then cooled to −78 °C. Anhydrous THF (80 mL) was added slowly into the reaction mixture to give a yellow suspension, which was stirred at −78 °C for 1 h. A solution of carboxaldehyde (0.9 equiv) in anhydrous THF (10 mL) was then introduced via syringe. The resulting reaction mixture was stirred at −78 °C for 1 h, after which time it was gradually warmed to room temperature and further stirred for 4 h. The mixture was diluted with hexanes (100 mL) and filtered under vacuum. The filtrate was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc/hexanes) to afford the desired vinyl bromide. The ratio of (*Z*):(*E*) isomers was determined by ^{1}H NMR spectroscopy.

3-(2-Bromovinyl)thiophene (S6)[31] ((*Z*):(*E*) = 4.3:1.0). Synthesized from (bromomethyl)triphenylphosphonium bromide (12.1 g, 27.8 mmol), KO^tBu (3.15 g, 28.1 mmol), and thiophene-3-carboxaldehyde (2.80 g, 25.0 mmol); EtOAc/hexanes = 1:20; 1.96 g, 10.4 mmol, 41%; pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 2.8 Hz, 1H), 7.47 (d, J = 5.2 Hz, 1H), 7.32−7.24 (ovrlp, 1.5H), 7.13−7.05 (ovrlp, 1.5H), 6.62 (d, J = 14.0 Hz, 0.23H), 6.22 (d, J = 8.0 Hz, 1H).

(5-(2-Bromovinyl)-1*H*-indol-1-yl)(phenyl)methanone (S7) ((*Z*):(*E*) = 20:1). Synthesized from (bromomethyl)triphenylphosphonium bromide (8.72 g, 20.0 mmol), KO^tBu (2.35 g, 21.0 mmol), and 1-benzoyl-1*H*-indole-5-carboxaldehyde[32] (4.49 g, 18.0 mmol); EtOAc/hexanes = 1:12; 3.68 g, 11.3 mmol, 63%; white solid. Mp: 66−68 °C. ^{1}H NMR of (*Z*) isomer (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 1H), 8.01 (s, 1H), 7.73 (d, J = 7.6 Hz, 2H), 7.65−7.58 (ovrlp, 2H), 7.52 (t, J = 8.0 Hz, 2H), 7.31 (d, J = 3.6 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 6.62 (d, J = 4.0 Hz, 1H), 6.43 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) 168.6, 135.7, 134.4, 132.6, 132.1, 130.8, 130.7, 129.3, 128.7, 128.3, 126.3, 121.4, 116.2, 108.8, 105.7. IR (neat cm^{-1}) δ 1673, 1468, 1444, 1371, 1323, 1184, 1065, 882, 825, 793, 771, 737, 720, 696, 606. Anal. Calcd for $C_{17}H_{12}BrNO$: C, 62.60; H, 3.71. Found: C, 62.79; H, 3.83.

Preparation of Enamides via Cu-Catalyzed Amidations of Vinyl Halides. Adapted from a previously reported procedure with some modification.[10] An oven-dried 25 mL resealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar was charged with vinyl halide (if solid), amide, CuI, and K_2CO_3. The tube was then evacuated and backfilled with argon (this sequence was repeated a total of three times). Vinyl halide (if liquid) and *N*,*N*′-dimethylethylenediamine (DMEDA) were added into the tube followed by anhydrous THF via syringe. The sealed tube was placed in a preheated oil bath (80 °C). After stirring at the same temperature for 18 h, the reaction mixture was allowed to cool to room temperature. The reaction mixture was then extracted with ethyl acetate (EtOAc) (20 mL) and deionized water (100 mL) in a separation funnel. The aqueous fraction was further extracted with EtOAc (2 × 10 mL). The combined organic fractions were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography using the indicated solvent system as an eluent to afford the enamide substrates.

(*E*)-*N*-Styrylbenzamide (1a).[33] Synthesized from (*E*)-(2-bromovinyl)benzene[21] (900 mg, 4.92 mmol, 1.0 equiv), benzamide (714 mg, 5.90 mmol, 1.2 equiv), K_2CO_3 (1.36 g, 9.84 mmol, 2.0 equiv), CuI (93.7 mg, 0.492 mmol, 10 mol %), DMEDA (212 μL, 1.97 mmol, 40 mol %), and THF (10.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 736 mg, 3.29 mmol, 67%; white solid. Mp: 178−180 °C (lit.: 172−173 °C).[33] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.67 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 7.2 Hz, 2H), 7.70 (dd, J = 14.8 Hz, 8.0 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 2H), 7.40 (d, J = 7.2 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 6.50 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 136.6, 133.4, 131.9, 128.8, 128.5, 127.7, 126.3, 125.3, 124.2, 113.0. IR (neat cm^{-1}) 3302, 1637, 1522, 1483, 1310, 1288, 1171, 1074, 953, 927, 746, 691.

(*E*)-4-Methoxy-*N*-styrylbenzamide (1b). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.28 g, 7.0 mmol, 1.0 equiv), 4-methoxybenzamide (1.27 g, 8.4 mmol, 1.2 equiv), K_2CO_3 (1.93 g, 14.0 mmol, 2.0 equiv), CuI (267 mg, 1.40 mmol, 20 mol %), DMEDA (301 μL, 2.80 mmol, 40 mol %), and THF (14.0 mL, 0.5 M); EtOAc/hexanes = 1:6, then 2:1; 1.09 g, 4.31 mmol, 62%; white solid. Mp: 190−192 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.49 (d, J = 10.0 Hz, 1H), 7.97 (d, J = 8.8 Hz, 2H), 7.66 (dd, J = 14.8 Hz, 10 Hz, 1H), 7.38 (d, J = 7.2 Hz, 2H), 7.30 (t, J = 7.2 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 7.06 (d, J = 8.8 Hz, 2H), 6.44 (d, J = 14.8 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.5, 162.2, 136.8, 129.6, 128.7, 126.1, 125.5, 125.2, 124.4, 113.7, 112.3, 55.4. IR (neat cm^{-1}) 3336, 1665, 1636, 1603, 1524, 1486, 1288, 1252, 1179, 1028, 949, 844, 749, 694, 668. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97. Found: C, 75.61; H, 5.84.

(*E*)-4-Methyl-*N*-styrylbenzamide (1c).[34] Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.10 g, 6.0 mmol, 1.0 equiv), 4-methylbenzamide (973 mg, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.20 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 960 mg, 4.05 mmol, 67%; off-white solid. Mp: 188−190 °C (lit.: 194−195 °C).[34] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.56 (d, J = 10.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.67 (dd, J = 14.8 Hz, 10.0 Hz, 1H), 7.40 (d, J = 7.2 Hz, 2H), 7.34−7.28 (ovrlp, 4H), 7.16 (t, J = 7.2 Hz, 1H), 6.47 (d, J = 14.8 Hz, 1H). 2.38 (s, 3H). ^{13}C

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NMR (100 MHz, DMSO-d_6) δ 163.9, 142.0, 136.7, 130.5, 129.1, 128.7, 127.7, 126.2, 125.2, 124.2, 112.6, 21.0. IR (neat cm^{-1}) 3219, 1624, 1523, 1485, 1309, 1285, 1185, 961, 835, 761, 737, 693, 636.

(*E*)-4-Chloro-*N*-styrylbenzamide (1d). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.10 g, 6.0 mmol, 1.2 equiv), 4-chlorobenzamide (778 mg, 5.0 mmol, 1.0 equiv), K_2CO_3 (1.38 g, 10.0 mmol, 2.0 equiv), CuI (191 mg, 1.0 mmol, 20 mol %), DMEDA (215 μL, 2.0 mmol, 40 mol %), and THF (10.0 mL, 0.5 M). EtOAc/hexanes = 1:7, then 1:4; 821 mg, 3.18 mmol, 64%; pale-yellow solid. Mp: 187−188 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.71 (d, J = 10.0 Hz, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.65 (dd, J = 14.8 Hz, 10.0 Hz, 1H), 7.61 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 7.2 Hz, 2H), 7.70 (t, J = 7.6 Hz, 2H), 7.17 (t J = 7.2 Hz, 1H), 6.48 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 136.8, 136.5, 132.1, 129.6, 128.7, 128.6, 126.3, 125.3, 124.0, 113.3. IR (neat cm^{-1}) 3330, 1641, 1523, 1479, 1279, 1171, 1091, 1013, 941, 843, 747, 692, 670. Anal. Calcd for $C_{15}H_{12}ClNO$: C, 69.91; H, 4.69. Found: C, 69.91; H, 4.75.

(*E*)-4-Fluoro-*N*-styrylbenzamide (1e). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.32 g, 7.2 mmol, 1.2 equiv), 4-fluorobenzamide (835 mg, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 813 mg, 3.37 mmol, 56%; off-white solid. Mp: 181−183 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.66 (d, J = 10.0 Hz, 1H), 8.07 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HF}$ = 5.6 Hz, 2H), 7.67 (dd, J = 14.4 Hz, 10.0 Hz, 1H), 7.40−7.34 (ovrlp, 4H), 7.30 (t, J = 8.0 Hz, 2H), 7.17 (t, J = 7.6 Hz, 1H), 6.48 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3 (d, $^1J_{CF}$ = 248.1 Hz), 163.0, 136.6, 130.4 (d, $^3J_{CF}$ = 9.1 Hz), 129.8 (d, $^4J_{CF}$ = 2.7 Hz), 128.7, 126.3, 125.3, 124.1, 115.5 (d, $^2J_{CF}$ = 21.7 Hz), 113.1. ^{19}F NMR (376 MHz, DMSO-d_6) δ −108.4. IR (neat cm^{-1}) 3343, 1642, 1599, 1525, 1483, 1286, 1222, 1158, 942, 846, 747, 692, 655, 624, 604. Anal. Calcd for $C_{15}H_{12}FNO$: C, 74.67; H, 5.01. Found: C, 74.85; H, 5.20.

(*E*)-*N*-Styryl-4-(trifluoromethyl)benzamide (1f). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (915 mg, 5.0 mmol, 1.5 equiv), 4-(trifluoromethyl)benzamide (630 mg, 3.33 mmol, 1.0 equiv), K_2CO_3 (921 mg, 6.67 mmol, 2.0 equiv), CuI (317 mg, 1.67 mmol, 50 mol %), DMEDA (215 μL, 2.0 mmol, 60 mol %), and THF (7.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 668 mg, 2.29 mmol, 69%; off-white solid. Mp: 206−208 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.86 (d, J = 10.0 Hz, 1H), 8.18 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.68 (dd, J = 14.8 Hz, 10.0 Hz, 1H), 7.42 (d, J = 7.6 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 6.52 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 137.1, 136.4, 131.7 (q, $^2J_{CF}$ = 31.7 Hz), 128.8, 128.6, 126.5, 125.5 (q, $^3J_{CF}$ = 3.3 Hz), 125.4, 123.91 (q, $^1J_{CF}$ = 270.6 Hz), 123.88, 113.8. ^{19}F NMR (376 MHz, DMSO-d_6) δ −61.7. IR (neat cm^{-1}) 3336, 1645, 1527, 1487, 1323, 1169, 1154, 1111, 1064, 1015, 941, 856, 770, 749, 688, 666. Anal. Calcd for $C_{16}H_{12}F_3NO$: C, 65.98; H, 4.15; Found: C, 65.75; H, 4.20.

(*E*)-4-Nitro-*N*-styrylbenzamide (1g). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.10 g, 6.0 mmol, 1.0 equiv), 4-nitrobenzamide (1.20 g, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:4, then 1:2; 609 mg, 2.27 mmol, 38%; yellow solid. Mp: 224−225 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.93 (d, J = 8.8 Hz, 1H), 8.36 (dd, J = 8.8 Hz, 1.6 Hz, 2H), 8.20 (dd, J = 8.8 Hz, 2.0 Hz, 2H), 7.64 (dd, J = 14.4 Hz, 9.6 Hz, 1H), 7.41 (d, J = 7.6 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 6.51 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.4, 149.3, 138.9, 136.3, 129.1, 128.7, 126.6, 125.4, 123.8, 123.6, 114.2. IR (neat cm^{-1}) 3306, 1636, 1598, 1518, 1482, 1310, 1285, 1170, 1109, 937, 865, 852, 749, 685. Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; Found: C, 67.04; H, 4.46.

(*E*)-3-Nitro-*N*-styrylbenzamide (1h).[35] Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.54 g, 8.4 mmol, 1.4 equiv), 3-nitrobenzamide (997 mg, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (572 mg, 3.0 mmol, 50 mol %), DMEDA (387 μL, 3.6 mmol, 60 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:5, then 1:2; 875 mg, 3.26 mmol, 54%; yellow solid. Mp: 180−181 °C. (lit.: 178−179 °C).[35] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.97 (d, J = 9.6 Hz, 1H), 8.81 (s, 1H), 8.43−8.39 (ovrlp, 2H), 7.82 (t, J = 8.0 Hz, 1H), 7.65 (dd, J = 14.4 Hz, 9.6 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 6.51 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.9, 147.8, 136.3, 134.7, 134.1, 130.3, 128.8, 126.5, 126.4, 125.4 123.8, 122.3, 114.0. IR (neat cm^{-1}) 3301, 1638, 1524, 1348, 1177, 1074, 944, 909, 864, 818, 750, 714, 692, 666.

(*E*)-*N*-(4-Methoxystyryl)benzamide (1i).[36] Synthesized from (*E*)-1-(2-bromovinyl)-4-methoxybenzene[21] (1.53 g, 7.2 mmol, 1.2 equiv), benzamide (727 mg, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (343 mg, 1.8 mmol, 30 mol %), DMEDA (387 μL, 3.6 mmol, 60 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:2, then 2:1. The isolated white solid was further purified by recrystallization from acetone/methanol/hexanes (~3:1:5) via slow evaporation with the aid of a rotary evaporator; 741 mg, 2.93 mmol, 49%; white solid. Mp: 192−193 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (d, J = 9.6 Hz, 1H), 7.97 (d, J = 7.2 Hz, 2H), 7.61−7.50 (ovrlp, 4H), 7.33 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 6.44 (d, J = 14.4 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.9, 158.0, 133.5, 131.8, 129.0, 128.5, 127.6, 126.5, 122.4, 114.2, 112.8, 55.1. IR (neat cm^{-1}) 3319, 1636, 1605, 1504, 1484, 1285, 1244, 1177, 1031, 942, 846, 811, 690, 664.

(*E*)-4-(2-Benzamidovinyl)phenyl Acetate (1j). Synthesized from (*E*)-4-(2-bromovinyl)phenyl acetate (**S1**) (1.86 g, 7.7 mmol, 1.1 equiv), benzamide (848 mg, 7.0 mmol, 1.0 equiv), K_2CO_3 (1.26 g, 9.1 mmol, 1.3 equiv), CuI (400 mg, 2.1 mmol, 30 mol %), DMEDA (452 μL, 4.2 mmol, 60 mol %), and THF (14.0 mL, 0.5 M); EtOAc/hexanes = 1:6, then 2:3. The isolated white solid was further purified by recrystallization from EtOAc/methanol (~3:1) via slow evaporation with the aid of a rotary evaporator; 474 mg, 1.69 mmol, 24%; white solid. Mp: 205−207 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.66 (d, J = 10.0 Hz, 1H), 7.98 (d, J = 7.2 Hz, 2H), 7.65 (dd, J = 14.8 Hz, 10.0 Hz, 1H), 7.61−7.51 (ovrlp, 3H), 7.43 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 6.48 (d, J = 14.4 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.3, 164.1, 148.9, 134.3, 133.3, 132.0, 128.5, 127.7, 126.2, 124.3, 122.1, 112.1, 20.9. IR (neat cm^{-1}) 3304, 1755, 1639, 1505, 1371, 1331, 1226, 1016, 949, 915, 796, 694. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37. Found: C, 72.39; H, 5.27.

(*E*)-*N*-(4-Methylstyryl)benzamide (1k).[13] Synthesized from (*E*)-1-(2-bromovinyl)-4-methylbenzene[21] (1.38 g, 7.0 mmol, 1.0 equiv), benzamide (1.02 mg, 8.4 mmol, 1.2 equiv), K_2CO_3 (1.93 g, 14.0 mmol, 2.0 equiv), CuI (267 mg, 1.4 mmol, 20 mol %), DMEDA (300 μL, 2.8 mmol, 40 mol %), and THF (14.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 1.18 g, 4.98 mmol, 71%; off-white solid. Mp: 174−176 °C (lit.: 178−179 °C).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (d, J = 9.6 Hz, 1H), 7.98 (d, J = 7.2 Hz, 2H), 7.66−7.57 (ovrlp, 2H), 7.53 (t, J = 7.6 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.45 (d, J = 14.8 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 135.5, 133.7, 133.4, 131.9, 129.4, 128.5, 127.6, 125.2, 123.4, 113.0, 20.8. IR (neat cm^{-1}) 3301, 1638, 1531, 1506, 1309, 1285, 1170, 956, 925, 794, 692. Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37. Found: C, 80.71; H, 6.41.

(*E*)-*N*-(4-Chlorostyryl)benzamide (1l). Synthesized from (*E*)-1-(2-bromovinyl)-4-chlorobenzene (1.31 g, 6.0 mmol, 1.0 equiv), benzamide (872 mg, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (286 mg, 1.5 mmol, 25 mol %), DMEDA (322 μL, 3.0 mmol, 50 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:3; 987 mg, 3.83 mmol, 64%; pale yellow solid. Mp: 181−183 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.68 (d, J = 10.0 Hz, 1H), 7.98 (d, J = 7.8 Hz, 2H), 7.68 (dd, J = 14.8 Hz, 10.0 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 8.0 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 6.45 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 135.7, 133.3, 132.0, 130.4, 128.6, 128.5, 127.7, 126.9, 125.0, 111.6. IR (neat cm^{-1}) 3338, 1634, 1516, 1479, 1326, 1298, 1275, 1166, 1091, 1010, 945, 852, 808, 716, 692, 657. Anal. Calcd for $C_{15}H_{12}ClNO$: C, 69.91; H, 4.69. Found: C, 69.82; H, 4.69.

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(*E*)-4-Bromo-*N*-(4-bromostyryl)benzamide (1m). Synthesized from (*E*)-1-bromo-4-(2-bromovinyl)benzene (**S2**) (2.20 g, 8.4 mmol, 1.4 equiv), 4-bromobenzamide (1.20 g, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:6, then 2:5. The isolated off-white solid was further purified by recrystallization from acetone/EtOAc/hexanes (~1:1:2) via slow evaporation with the aid of a rotary evaporator; 1.02 g, 2.67 mmol, 45%; off-white solid. Mp: 227−230 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.74 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 2H), 7.74 (d, *J* = 7.6 Hz, 2H), 7.67 (dd, *J* = 14.0 Hz, 10.0 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 7.6 Hz, 2H), 6.43 (d, *J* = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.1, 135.9, 132.3, 131.5, 129.7, 127.3, 125.8, 124.9, 118.9, 112.0. IR (neat cm^{-1}) 3309, 1639, 1588, 1521, 1477, 1334, 1274, 1170, 1072, 1008, 946, 938, 839, 804, 753, 700, 679. Anal. Calcd for $C_{15}H_{11}Br_2NO$: C, 47.28; H, 2.91. Found: C, 47.03; H, 2.85.

(*E*)-4-(*tert*-Butyl)-*N*-(4-fluorostyryl)benzamide (1n). Synthesized from (*E*)-1-(2-bromovinyl)-4-fluorobenzene (**S3**) (1.21 g, 6.0 mmol, 1.0 equiv), 4-(*tert*-butyl)benzamide (1.28 g, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 755 mg, 2.54 mmol, 42%; off-white solid. Mp: 181−182 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (d, *J* = 9.6 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.62 (dd, *J* = 14.4 Hz, 9.6 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.43 (dd, $^3J_{HH}$ = 8.8 Hz, $^4J_{HF}$ = 5.6 Hz, 2H), 7.12 (dd, $^3J_{HH}$ = 8.8 Hz, $^3J_{HF}$ = 8.8 Hz, 2H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.9, 160.8 (d, $^1J_{CF}$ = 241.5 Hz), 154.8, 133.2 (d, $^4J_{CF}$ = 3.1 Hz), 130.6, 127.5, 126.9 (d, $^3J_{CF}$ = 8.7 Hz), 125.2, 124.2, 115.5 (d, $^2J_{CF}$ = 21.4 Hz), 111.6, 34.7, 30.9. ^{19}F NMR (376 MHz, DMSO-d_6) δ −115.9. IR (neat cm^{-1}) 3243, 2968, 1633, 1532, 1495, 1319, 1302, 1283, 1233, 1171, 1155, 962, 852, 816, 749, 700. Anal. Calcd for $C_{19}H_{20}FNO$: C, 76.74; H, 6.78. Found: C, 76.55; H, 6.91.

(*E*)-*N*-(3,4-Difluorostyryl)-3,4,5-trimethoxybenzamide (1o). Synthesized from (*E*)-4-(2-bromovinyl)-1,2-difluorobenzene (**S4**) (1.84 g, 8.4 mmol, 1.2 equiv), 3,4,5-trimethoxybenzamide (1.48 g, 7.0 mmol, 1.0 equiv), K_2CO_3 (1.93 g, 14.0 mmol, 2.0 equiv), CuI (400 mg, 2.1 mmol, 30 mol %), DMEDA (451 μL, 4.2 mmol, 60 mol %), and THF (14.0 mL, 0.5 M); EtOAc/hexanes = 1:6, then 2:5; 1.27 g, 3.64 mmol, 52%; white solid. Mp: 158−159 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (d, *J* = 9.6 Hz, 1H), 7.66 (dd, *J* = 14.8 Hz, 9.6 Hz, 1H), 7.53−7.48 (m, 1H), 7.35−7.28 (ovrlp, 3H), 7.23 (br, 1H), 6.41 (d, *J* = 14.8 Hz, 1H), 3.87 (s, 6H), 3.73 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.6, 152.7, 149.9 (dd, $^1J_{CF}$ = 243.1 Hz, $^2J_{CF}$ = 12.7 Hz), 148.0 (dd, $^1J_{CF}$ = 243.5 Hz, $^2J_{CF}$ = 12.8 Hz), 140.7, 134.7 (dd, $^3J_{CF}$ = 6.2 Hz, $^4J_{CF}$ = 3.6 Hz), 128.3, 125.7, 122.0 (dd, $^3J_{CF}$ = 6.2 Hz, $^4J_{CF}$ = 2.9 Hz), 117.6 (d, $^2J_{CF}$ = 17.2 Hz), 113.7 (d, $^2J_{CF}$ = 17.5 Hz), 110.9, 105.3, 60.1, 56.1. ^{19}F NMR (376 MHz, DMSO-d_6) δ −138.3, −141.4. IR (neat cm^{-1}) 3286, 1638, 1581, 1493, 1413, 1337, 1234, 1124, 995, 942, 868, 847, 814, 754, 708, 674. Anal. Calcd for $C_{18}H_{17}F_2NO_4$: C, 61.89; H, 4.91. Found: C, 61.91; H, 5.00.

(*E*)-2-Methyl-*N*-(2-methylstyryl)benzamide (1p). Synthesized from (*E*)-1-(2-bromovinyl)-2-methylbenzene (**S5**) (1.18 g, 6.0 mmol, 1.0 equiv), 2-methylbenzamide (973 mg, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (343 mg, 1.8 mmol, 30 mol %), DMEDA (397 μL, 3.6 mmol, 60 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7; then 1:4; 890 mg, 3.54 mmol, 59%; white solid. Mp: 184−185 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (d, *J* = 10.0 Hz, 1H), 7.54−7.47 (ovrlp, 3H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.31−7.28 (ovrlp, 2H), 7.18−7.15 (ovrlp, 2H), 7.09 (t, *J* = 7.2 Hz, 1H), 6.56 (d, *J* = 14.8 Hz, 1H), 2.41 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.5, 135.9, 135.6, 135.1, 134.1, 130.7, 130.2, 130.0, 127.4, 126.2, 126.2, 125.6, 124.3, 124.0, 110.3, 19.5. IR (neat cm^{-1}) 3263, 1637, 1517, 1471, 1322, 1281, 1170, 1098, 946, 782, 742, 729, 703, 663. Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82. Found: C, 81.02; H, 6.81.

(*E*)-*N*-(2-Methylstyryl)-2-naphthamide (1q). Synthesized from (*E*)-1-(2-bromovinyl)-2-methylbenzene (**S5**) (1.66 g, 8.4 mmol, 1.2 equiv), 2-naphthamide (1.20 g, 7.0 mmol, 1.0 equiv), K_2CO_3 (1.93 g, 14.0 mmol, 2.0 equiv), CuI (400 mg, 2.1 mmol, 30 mol %), DMEDA (452 μL, 4.2 mmol, 60 mol %), and THF (14.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:3; 1.23 g, 4.27 mmol, 61%; off-white solid. Mp: 179−181 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (d, *J* = 9.6 Hz, 1H), 8.64 (s, 1H), 8.10−8.04 (ovrlp, 3H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.68−7.60 (ovrlp, 3H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.18−7.15 (ovrlp, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 14.4 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 135.3, 134.4, 134.2, 132.1, 130.7, 130.3, 129.0, 128.2, 128.1, 128.0, 127.7, 126.9, 126.3, 124.7, 124.2, 124.0, 110.6, 19.6. IR (neat cm^{-1}) 3275, 1636, 1521, 1478, 1327, 1286, 1239, 1089, 951, 822, 741, 718. Anal. Calcd for $C_{20}H_{17}NO$: C, 83.59; H, 5.96. Found: C, 83.41; H, 6.04.

***N*-((*E*)-Styryl)cinnamamide (3a).**[33] Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.32 g, 7.2 mmol, 1.2 equiv), *trans*-cinnamamide (883 mg, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:4, then 2:1; 1.31 g, 5.26 mmol, 88%; yellow solid. Mp: 196−198 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.50 (d, *J* = 10.0 Hz, 1H), 7.65−7.57 (ovrlp, 4H), 7.46−7.38 (ovrlp, 5H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.74 (d, *J* = 16.0 Hz, 1H), 6.28 (d, *J* = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 140.6, 136.5, 134.6, 129.9, 129.0, 128.7, 127.8, 126.2, 125.2, 123.8, 120.9, 112.2. IR (neat cm^{-1}) 3373, 3159, 3027, 1635, 1606, 1520, 1341, 1234, 1195, 983, 957, 748, 679.

***N*-((1*E*,3*E*)-4-Phenylbuta-1,3-dien-1-yl)benzamide (3b).** Synthesized from ((1*E*)-4-bromobuta-1,3-dien-1-yl)benzene ((3*Z*): (3*E*) = 2.6: 1.0)[23] (3.76 g, 18.0 mmol, 3.0 equiv), benzamide (727 mg, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 1.13 g, 4.53 mmol, 70%; yellow solid. Mp: 179−181 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.62 (d, *J* = 10.0 Hz, 1H), 7.97 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.2 Hz, 2H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.36 (dd, *J* = 13.6 Hz, 10.4 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.03 (dd, *J* = 15.2 Hz, 11.2 Hz, 1H), 6.49 (d, *J* = 15.6 Hz, 1H), 6.36 (dd, *J* = 13.2 Hz, 11.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.8, 137.6, 133.3, 131.9, 128.6, 128.5, 128.4, 128.1, 128.0, 127.6, 126.7, 125.8, 114.3. IR (neat cm^{-1}) 3328, 3060, 1634, 1510, 1485, 1444, 1340, 1300, 1264, 1150, 1072, 968, 908, 795, 744, 688. HRMS (ESI) calcd for $C_{17}H_{15}NO$ [M + H]: 250.1226; found 250.1235.

(*E*)-3-(3,4-Dimethoxyphenyl)-*N*-((*E*)-4-methoxystyryl)-acrylamide (3c). Synthesized from (*E*)-1-(2-bromovinyl)-4-methoxybenzene[21] (1.41 g, 6.6 mmol, 1.1 equiv), (*E*)-3-(3,4-dimethoxyphenyl)acrylamide[24] (1.24 g, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (343 mg, 1.8 mmol, 30 mol %), DMEDA (387 μL, 3.6 mmol, 60 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1: 4, then 4:1. The isolated yellow solid was further purified by recrystallization from acetone/EtOAc/hexanes (~1:1:2) via slow evaporation with the aid of a rotary evaporator; 1.31 g, 3.87 mmol, 64%; yellow solid. Mp: 195−197 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (d, *J* = 10.4 Hz, 1H), 7.54 (d, *J* = 15.6 Hz, 1H), 7.45 (dd, *J* = 14.8 Hz, 10.4 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 1.6 Hz, 1H), 7.18 (dd, *J* = 8.4 Hz, 1.6 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.59 (d, *J* = 15.6 Hz, 1H), 6.20 (d, *J* = 14.8 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 157.9, 150.5, 148.9, 140.4, 129.1, 127.5, 126.4, 122.1, 121.7, 118.6, 114.2, 111.8, 111.7, 110.2, 55.5, 55.4, 55.0. IR (neat cm^{-1}) 3260, 1640, 1622, 1503, 1440, 1339, 1240, 1190, 1137, 1020, 964, 947, 845, 807, 691, 585. Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24. Found: C, 70.48; H, 6.13.

(*E*)-*N*-(Dec-1-en-1-yl)benzamide (3d). Synthesized from (*E*)-1-iododec-1-ene[22] (2.24 g, 8.4 mmol, 1.2 equiv), benzamide (848 mg, 7.0 mmol, 1.0 equiv), K_2CO_3 (1.93 g, 14.0 mmol, 2.0 equiv), CuI (267 mg, 1.4 mmol, 20 mol %), DMEDA (301 μL, 2.80 mmol, 40 mol %), and THF (14.0 mL, 0.5 M) at 70 °C; EtOAc/hexanes = 1:10, then 1:7; 1.19 g, 4.6 mmol, 66%; white solid. Mp: 69−70 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.14 (d, *J* = 9.6 Hz, 1H), 7.91 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 6.83 (dd, *J* =

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14.4 Hz, 9.6 Hz, 1H), 5.46 (dt, J = 14.4 Hz, 7.2 Hz, 1H), 2.02 (td, J = 6.9 Hz, 6.8 Hz, 2H), 1.35−1.25 (ovrlp, 12H), 0.85 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.5, 133.7, 131.5, 128.3, 127.4, 123.6, 113.3, 31.3, 29.61, 29.56, 28.9, 28.7, 28.6, 22.1, 13.9. IR (neat cm^{-1}) 3322, 2922, 2850, 1636, 1518, 1488, 1326, 1294, 1260, 1185, 961, 857, 795, 725, 692, 638. Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71. Found: C, 78.91; H, 9.62.

(*E*)-*N*-Styrylpivalamide (3e).[37] Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.10 g, 6.0 mmol, 1.0 equiv), pivalamide (728 mg, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.70 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (259 μL, 2.4 mmol, 40 mol %), and THF (6.0 mL, 1.0 M); EtOAc/hexanes = 1:10; 974 mg, 4.79 mmol, 80%; white solid. Mp: 146−147 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.65 (d, J = 10.0 Hz, 1H), 7.45 (dd, J = 14.8 Hz, 10.0 Hz, 1H), 7.31 (d, J = 7.2 Hz, 2H), 7.27 (t, J = 7.2 Hz, 2H), 7.22 (t, J = 7.2 Hz, 1H), 6.33 (d, J = 14.8 Hz, 1H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.6, 136.9, 128.7, 125.9, 125.0, 124.4, 111.4, 38.3, 27.0. IR (neat cm^{-1}) 3279, 2973, 1632, 1524, 1474, 1398, 1303, 1285, 1235, 1183, 952, 746, 718, 691.

(*E*)-*N*-Styrylcyclohexanecarboxamide (3f).[35] Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.10 g, 6.0 mmol, 1.0 equiv), cyclohexanecarboxamide (916 mg, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (6.0 mL, 1.0 M); EtOAc/hexanes = 1: 10, then 1:7; 869 mg, 3.79 mmol, 63%; white solid. Mp: 151−152 °C. (lit.: 148−150 °C).[35] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (d, J = 10.4 Hz, 1H), 7.41 (dd, J = 14.8 Hz, 10.4 Hz, 1H), 7.31 (d, J = 7.2 Hz, 2H), 7.26 (t, J = 7.2 Hz, 2H), 7.12 (t, J = 7.2 Hz, 1H), 6.15 (d, J = 14.8 Hz, 1H), 2.23 (m, 1H), 1.77−1.72 (ovrlp, 4H), 1.63 (d, J = 8.8 Hz, 1H), 1.43−1.35 (m, 2H), 1.29−1.12 (ovrlp, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.3, 136.8, 128.6, 125.9, 125.0, 123.9, 111.0, 43.9, 29.0, 25.4, 15.2. IR (neat cm^{-1}) 3262, 2933, 2850, 1665, 1634, 1536, 1444, 1252, 1227, 1194, 956, 748, 718, 688.

(*E*)-*N*-(2-(Thiophen-3-yl)vinyl)benzamide (3g). Synthesized from 3-(2-bromovinyl)thiophene ((Z):(E) = 4.3: 1.0) (**S6**) (1.96 g, 10.4 mmol, 2.1 equiv), benzamide (606 mg, 5.0 mmol, 1.0 equiv), K_2CO_3 (1.38 g, 10.0 mmol, 2.0 equiv), CuI (191 mg, 1.0 mmol, 20 mol %), DMEDA (215 μL, 2.0 mmol, 40 mol %), and THF (10.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 821 mg, 3.58 mmol, 72%; off-white solid. Mp: 147−149 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.54 (d, J = 10.0 Hz, 1H), 7.97 (d, J = 7.2 Hz, 2H), 7.61−7.49 (ovrlp, 5H), 7.36 (d, J = 2.4 Hz, 1H), 7.33 (d, J = 4.8 Hz, 1H), 6.52 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 138.5, 133.5, 131.8, 128.5, 127.6, 126.7, 124.7, 124.1, 120.1, 108.3. IR (neat cm^{-1}) 3308, 1638, 1539, 1506, 1485, 1316, 1250, 1200, 952, 926, 771, 726, 672, 627. Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.09; H, 4.84. Found: C, 67.81; H, 4.72.

(*E*)-*N*-Styrylthiophene-3-carboxamide (3h). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.32 g, 7.2 mmol, 1.2 equiv), thiophene-3-carboxamide (763 mg, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 990 mg, 4.32 mmol, 72%; off-white solid. Mp: 166−167 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (d, J = 9.6 Hz, 1H), 8.35 (dd, J = 2.4 Hz, 1.6 Hz, 1H), 7.66−7.60 (ovrlp, 3H), 7.39 (d, J = 7.2 Hz, 2H), 7.30 (t, J = 7.6 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 6.42 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 136.63, 136.60, 130.2, 128.8, 127.2, 127.0, 126.2, 125.2, 123.9, 112.5. IR (neat cm^{-1}) 3230, 1619, 1531, 1486, 1304, 1283, 1262, 1165, 1071, 956, 853, 813, 721, 691. Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.09; H, 4.84. Found: C, 67.88; H, 4.75.

(*E*)-*N*-Styrylthiophene-2-carboxamide (3i). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.32 g, 7.2 mmol, 1.2 equiv), thiophene-2-carboxamide (763 mg, 6.0 mmol, 1.0 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (258 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 856 mg, 3.73 mmol, 62%; off-white solid. Mp: 154−155 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.66 (d, J = 9.6 Hz, 1H), 7.99 (d, J = 3.6 Hz, 1H), 7.86 (d, J = 4.8 Hz, 1H), 7.60 (dd, J = 14.8 Hz, 9.6 Hz, 1H), 7.39 (d, J = 7.2 Hz, 2H), 7.30 (t, J = 7.2 Hz, 2H), 7.23 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.44 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.8, 138.8, 136.5, 132.2, 129.3, 128.7, 128.2, 126.3, 125.3, 123.7, 112.7. IR (neat cm^{-1}) 3223, 1615, 1526, 1487, 1413, 1353, 1307, 1288, 1171, 958, 850, 757, 719, 690. Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.09; H, 4.84. Found: C, 67.83; H, 4.81.

(*E*)-*N*-Styrylfuran-2-carboxamide (3j). Synthesized from (*E*)-(2-bromovinyl)benzene[21] (1.10 g, 6.0 mmol, 1.0 equiv), furan-2-carboxamide (800 mg, 7.2 mmol, 1.2 equiv), K_2CO_3 (1.66 g, 12.0 mmol, 2.0 equiv), CuI (229 mg, 1.2 mmol, 20 mol %), DMEDA (259 μL, 2.4 mmol, 40 mol %), and THF (12.0 mL, 0.5 M); EtOAc/hexanes = 1:7, then 1:4; 843 mg, 3.95 mmol, 66%; off-white solid. Mp: 184−185 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.62 (d, J = 9.6 Hz, 1H), 7.94 (s, 1H), 7.59 (dd, J = 14.8 Hz, 10.0 Hz, 1H), 7.38−7.27 (ovrlp, 5H), 7.15 (t, J = 7.2 Hz, 1H), 6.69 (m, 1H), 6.48 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.2, 147.0, 146.0, 136.5, 128.7, 126.3, 125.3, 123.1, 115.1, 113.1, 112.3. IR (neat cm^{-1}) 3205, 1628, 1584, 1519, 1486, 1465, 1308, 1263, 1177, 1018, 961, 863, 739, 689. Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20. Found: C, 72.95; H, 5.06.

(*E*)-*N*-(2-(1-Benzoyl-1*H*-indol-5-yl)vinyl)thiophene-3-carboxamide (3k). Synthesized from 5-(2-bromovinyl)-1*H*-indol-1-yl)-(phenyl)methanone ((*Z*):(*E*) = 20:1) (**S7**) (1.17 g, 3.59 mmol, 1.2 equiv), thiophene-3-carboxamide (380 mg, 2.99 mmol, 1.0 equiv), K_2CO_3 (826 mg, 5.98 mmol, 2.0 equiv), CuI (171 mg, 0.90 mmol, 30 mol %), DMEDA (194 μL, 1.8 mmol, 60 mol %), and THF (6.0 mL, 0.5 M); EtOAc/hexanes = 1:5, then 1:2. 310 mg, 0.83 mmol, 28%; pale yellow solid. Mp: 208−210 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.49 (d, J = 10.0 Hz, 1H), 8.36 (s, 1H), 8.21 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 8.0 Hz, 2H), 7.71−7.66 (ovrlp, 5 H), 7.59 (t, J = 7.6 Hz, 2H), 7.45 (d, J = 8.8 Hz, 1H), 7.35 (d, J = 3.6 Hz, 1H), 6.71 (d, J = 3.6 Hz, 1H), 6.55 (d, J = 14.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.0, 159.6, 136.7, 134.1, 134.0, 132.6, 132.0, 131.2, 130.1, 129.0, 128.7, 128.6, 127.1, 127.0, 123.4, 122.1, 117.6, 116.1, 112.8, 108.6. IR (neat cm^{-1}) 3274, 1679, 1633, 1527, 1459, 1367, 1335, 1285, 1190, 1067, 945, 881, 806, 766, 697. Anal. Calcd for $C_{22}H_{16}N_2O_2S$: C, 70.95; H, 4.33. Found: C, 70.65; H, 4.59.

General Procedure for the Optimization of Cu(II)-Catalyzed Oxidative Cyclization of Enamide (Table 1). A oven-dried 20 mL resealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar was charged with (*E*)-*N*-styrylbenzamide (**1a**) (0.2 mmol, 1.0 equiv), tetrabutylammonium halide (TBAB or TBAC) (0.24 mmol, 1.2 equiv), potassium persulfate ($K_2S_2O_8$) (0.26 mmol, 1.3 equiv), metal catalyst (5−20 mol %), and ligand (0−40 mol %) (if solid). The tube was then evacuated and backfilled with argon (this sequence was repeated a total of three times). Ligand (0−40 mol %) (if liquid) was added into the tube followed by anhydrous acetonitrile (2.0 mL, 0.1 M) via syringe. The sealed tube was then vigorously stirred at room temperature for 24 h. After completion, *n*-dodecane (20 μL, 0.088 mol) was added into the reaction mixture. The reaction mixture was extracted with ethyl acetate (3 mL) and deionized water (10 mL). Aliquots from the organic fractions were filtered through silica gel for GC analysis to determine the reaction conversion and the GC yield of 2,5-diphenyloxazole **2a** using *n*-dodecane as an internal standard. The aqueous fraction was further washed with ethyl acetate (2 × 3 mL). The combined organic fractions were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography using ethyl acetate (EtOAc)/hexanes (1:12) as an eluent to afford **2a** to determine the isolated yield.

General Procedure for Synthesis of Oxazoles via Cu(II)-Catalyzed Oxidative Cyclization of Enamides (Tables 2 and 3). Unless otherwise noted, an oven-dried 25 mL resealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar was charged with enamide (**1a−q**, **3a−k**) (1.0 mmol, 1.0 equiv), copper(II) bromide ($CuBr_2$) (16.8 mg, 0.075 mml, 7.5 mol %), tetrabutylammonium bromide (TBAB) (387 mg, 1.2 mmol, 1.2 equiv), and potassium persulfate ($K_2S_2O_8$) (351 mg, 1.3 mmol, 1.3 equiv). The tube was then evacuated and backfilled with argon (this sequence was repeated a total of three times). Ethyl nicotinate (20.5 μL, 0.15 mmol, 15 mol %) was added into the tube followed by anhydrous acetonitrile (10.0 mL,

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0.1 M) via syringe. The sealed tube was then vigorously stirred at room temperature for 24 h. After completion, the reaction mixture was extracted with ethyl acetate (10 mL) and deionized water (20 mL). The aqueous fraction was further washed with ethyl acetate (2 × 5 mL). The combined organic fractions were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography using ethyl acetate (EtOAc)/hexanes as an eluent to afford the oxazole products.

2,5-Diphenyloxazole (2a).[38] Synthesized from (*E*)-*N*-styrylbenzamide (**1a**) (233 mg); EtOAc/hexanes = 1:12; 175 mg, 79%; white solid. Mp: 70−71 °C (lit.: 70−71 °C).[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 8.0 Hz, 2H), 7.46−7.36 (ovrlp, 6H), 7.28 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 151.2, 130.3, 128.9, 128.8, 128.4, 128.0, 127.5, 126.3, 124.2, 123.5. IR (neat cm^{-1}) 1480, 1446, 1133, 1058, 952, 822, 775, 759, 705, 684. Anal. Calcd for $C_{15}H_{11}NO$: C, 81.43; H, 5.01. Found: C, 81.39; H, 5.10.

2-(4-Methoxyphenyl)-5-phenyloxazole (2b).[13] Synthesized from (*E*)-4-methoxy-*N*-styrylbenzamide (**1b**) (253 mg); EtOAc/hexanes = 1:10, then 1:8; 181 mg, 72%; white solid. Mp: 100−101 °C (lit.: 94−96 °C).[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.8 Hz, 2H), 7.66 (d, J = 7.6 Hz, 2H), 7.41−7.37 (ovrlp, 3H), 7.28 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 161.2, 150.7, 128.9, 128.2, 127.9, 124.0, 123.3, 120.3, 114.2, 55.3. IR (neat cm^{-1}) 1610, 1495, 1303, 1250, 1173, 1135, 1024, 828, 762, 736, 687, 615. Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21. Found: C, 76.29; H, 5.33.

5-Phenyl-2-(*p*-tolyl)oxazole (2c).[38] Synthesized from (*E*)-4-methyl-*N*-styrylbenzamide (**1c**) (237 mg); EtOAc/hexanes = 1:10; 171 mg, 73%; white solid. Mp: 73 °C (lit.: 72−73 °C).[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 7.8 Hz, 2H), 7.41−7.37 (ovrlp, 3H), 7.28 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 150.9, 140.6, 129.5, 128.9, 128.3, 128.1, 126.2, 124.8, 124.1, 123.3, 21.5. IR (neat cm^{-1}) 1495, 1134, 950, 822, 760, 730, 703, 688. Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57. Found: C, 81.79; H, 5.69.

2-(4-Chlorophenyl)-5-phenyloxazole (2d).[39] Synthesized from (*E*)-4-chloro-*N*-styrylbenzamide (**1d**) (258 mg); EtOAc/hexanes = 1:10; 187 mg, 73%; white solid. Mp: 116−118 °C (lit.: 115−117 °C).[39] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.8 Hz, 2H), 7.64 (d, J = 7.2 Hz, 2H), 7.41−7.33 (ovrlp, 5H), 7.23 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 151.4, 136.3, 129.1, 128.9, 128.6, 127.8, 127.5, 125.9, 124.2, 123.5. IR (neat cm^{-1}) 1477, 1403, 1132, 1087, 1009, 950, 824, 761, 731, 689. Anal. Calcd for $C_{15}H_{10}ClNO$: C, 70.46; H, 3.94. Found: C, 70.17; H, 3.82.

2-(4-Fluorophenyl)-5-phenyloxazole (2e).[38] Synthesized from (*E*)-4-fluoro-*N*-styrylbenzamide (**1e**) (241 mg). EtOAc/hexanes = 1:10; 170 mg, 71%; off-white solid. Mp: 84−85 °C (lit.: 81−82 °C).[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, $^3J_{HH}$ = 8.8 Hz, $^4J_{HF}$ = 5.2 Hz, 2H), 7.64 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 7.41−7.37 (ovrlp, 3H), 7.29 (t, $^3J_{HH}$ = 7.2 Hz, 1H), 7.11 (dd, $^3J_{HH}$ = 8.8 Hz, $^3J_{HF}$ = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (d, $^1J_{CF}$ = 249.4 Hz), 160.3, 151.3, 128.9, 128.5, 128.3 (d, $^3J_{CF}$ = 8.6 Hz), 127.9, 124.1, 123.8 (d, $^4J_{CF}$ = 3.0 Hz), 123.4, 116.0 (d, $^2J_{CF}$ = 21.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.8. IR (neat cm^{-1}) 1608, 1494, 1414, 1220, 1134, 952, 842, 756, 732, 685, 614. Anal. Calcd for $C_{15}H_{10}FNO$: C, 75.30; H, 4.21. Found: C, 75.08; H, 4.32.

5-Phenyl-2-(4-(trifluoromethyl)phenyl)oxazole (2f).[39] Synthesized from (*E*)-*N*-styryl-4-(trifluoromethyl)benzamide (**1f**) (233 mg, 0.80 mmol, 1.0 equiv), $CuBr_2$ (13.4 mg, 0.06 mmol, 7.5 mol %), TBAB (310 mg, 0.96 mmol, 1.2 equiv), $K_2S_2O_8$ (281 mg, 1.04 mmol, 1.3 equiv), ethyl nicotinate (16.4 μL, 0.12 mmol, 15 mol %), and acetonitrile (8.0 mL, 0.1 M). EtOAc/hexanes = 1:10; 166 mg, 0.57 mmol, 72%; white solid. Mp: 110−111 °C (lit.: 109−111 °C).[39] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 7.69−7.65 (ovrlp, 4H), 7.43−7.39 (ovrlp, 3H), 7.32 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 152.1, 131.8 (q, $^2J_{CF}$ = 32.6 Hz), 130.6, 129.0, 128.9, 127.7, 126.4, 125.9 (q, $^3J_{CF}$ = 3.5 Hz), 124.4, 124.0 (q, $^1J_{CF}$ = 270.7 Hz), 123.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.3. IR (neat cm^{-1}) 1485, 1414, 1324, 1168, 1102, 1055, 951, 843, 762, 750, 709, 691, 594. Anal. Calcd for $C_{16}H_{10}F_3NO$: C, 66.44; H, 3.48. Found: C, 66.19; H, 3.50.

2-(4-Nitrophenyl)-5-phenyloxazole (2g).[40] Synthesized from (*E*)-4-nitro-*N*-styrylbenzamide (**1g**) (268 mg); EtOAc/hexanes = 1:9; 58 mg, 22%; yellow solid. Mp: 201−203 °C (lit.: 207−208 °C).[40] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.8 Hz, 2H), 8.27 (d, J = 8.8 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.54 (s, 1H), 7.48 (t, J = 8.0 Hz, 2H), 7.40 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 153.0, 148.7, 133.0, 129.33, 129.25, 127.5, 127.0, 124.7, 124.44, 124.41. IR (neat cm^{-1}) 1537, 1514, 1339, 1103, 951, 853, 822, 765, 709, 690. Anal. Calcd for $C_{15}H_{10}N_2O_3$: 67.67; H, 3.79. Found: C, 67.26; H, 4.10.

2-(3-Nitrophenyl)-5-phenyloxazole (2h).[41] Synthesized from (*E*)-3-nitro-*N*-styrylbenzamide (**1h**) (268 mg); EtOAc/hexanes = 1:9; 116 mg, 44%; pale yellow solid. Mp: 148−149 °C (lit.: 148−150 °C).[41] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (t, J = 1.6 Hz, 1H), 8.40 (dt, J = 7.6 Hz, 1.6 Hz, 1H), 8.28 (ddd, J = 8.0 Hz, 2.4 Hz, 1.2 Hz, 1H), 7.73 (d, J = 7.2 Hz, 2H), 7.66 (t, J = 8.0 Hz, 1H), 7.48−7.45 (ovrlp, 3H), 7.38 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 152.4, 148.7, 131.8, 130.1, 129.11, 129.07, 129.00, 127.4, 124.6, 124.4, 123.9, 121.1. IR (neat cm^{-1}) 1519, 1352, 1135, 940, 816, 768, 742, 710. Anal. Calcd for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79. Found: C, 67.39, H, 4.02.

5-(4-Methoxyphenyl)-2-phenyloxazole (2i).[39] Synthesized from (*E*)-*N*-(4-methoxystyryl)benzamide (**1i**) (253 mg); EtOAc/hexanes = 1:10; 108 mg, 43%; off-white solid. Mp: 80−81 °C (lit.: 78−79 °C).[39] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 2H), 7.59 (d, J = 8.8 Hz, 2H), 7.46−7.38 (ovrlp, 3H), 7.29 (s, 1H), 6.92 (d, J = 8.8 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 159.8, 151.3, 130.1, 128.8, 127.6, 126.1, 125.7, 121.9, 120.8, 114.4, 55.3. IR (neat cm^{-1}) 1618, 1502, 1255, 1175, 1058, 1026, 951, 822, 813, 770, 713, 690. Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21. Found: C, 76.19; H, 5.35.

4-(2-Phenyloxazol-5-yl)phenyl Acetate (2j). Synthesized from (*E*)-4-(2-benzamidovinyl)phenyl acetate (**1j**) (281 mg); EtOAc/hexanes = 1:10, then 1:5; 226 mg, 81%; off-white solid. Mp: 113−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.8 Hz, 2H), 7.50−7.43 (ovrlp, 3H), 7.41 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 161.3, 150.7, 150.6, 130.5, 128.9, 127.4, 126.3, 125.9, 125.4, 123.6, 122.3, 21.2. IR (neat cm^{-1}) 1748, 1500, 1485, 1373, 1225, 1207, 1167, 1136, 1016, 953, 915, 844. HRMS (ESI) calcd for $C_{17}H_{13}NO_3$ [M+H]: 280.0968; found 280.0966.

2-Phenyl-5-(*p*-tolyl)oxazole (2k).[13] Synthesized from (*E*)-*N*-(4-methylstyryl)benzamide (**1k**) (237 mg). EtOAc/hexanes = 1:10; 124 mg, 53%; off-white solid. Mp: 77−78 °C (lit.: 77−78 °C).[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.4 Hz, 2H), 7.46−7.40 (ovrlp, 3H), 7.35 (s, 1H), 7.19 (d, J = 8.0 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 151.4, 138.4, 130.2, 129.6, 128.8, 127.6, 126.2, 125.3, 124.1, 122.8, 21.4. IR (neat cm^{-1}) 1543, 1500, 1476, 1446, 1133, 1055, 952, 817, 775, 709, 693, 504, 490. Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57. Found: C, 81.43; H, 5.81.

5-(4-Chlorophenyl)-2-phenyloxazole (2l).[13] Synthesized from (*E*)-*N*-(4-chlorostyryl)benzamide (**1l**) (258 mg); EtOAc/hexanes = 1:10; 175 mg, 69%; pale yellow solid. Mp: 104−105 °C (lit.: 102−104 °C).[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.45−7.39 (ovrlp, 3H), 7.36 (s, 1H), 7.33 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 150.2, 134.1, 130.4, 129.1, 128.8, 127.2, 126.5, 126.3, 125.3, 123.8. IR (neat cm^{-1}) 1480, 1448, 1132, 1091, 1011, 951, 818, 772, 705, 686. Anal. Calcd for $C_{15}H_{10}ClNO$: C, 70.46; H, 3.94. Found: C, 70.76; H, 3.84.

2,5-Bis(4-bromophenyl)oxazole (2m). Synthesized from (*E*)-4-bromo-*N*-(4-bromostyryl)benzamide (**1m**) (381 mg). EtOAc/hexanes = 1:10; 287 mg, 76%; white solid. Mp: 176−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.57 (s, 4H), 7.44 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 150.7, 132.34, 132.29, 127.9, 126.9, 126.3, 125.8, 125.1, 124.2, 122.7. IR (neat cm^{-1}) 1474, 1404, 1133, 1073, 1051, 1006, 950, 821, 730,

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697. Anal. Calcd for $C_{15}H_9Br_2NO$: C, 47.53; H, 2.39. Found: C, 47.17; H, 2.35.

2-(4-(*tert*-Butyl)phenyl)-5-(4-fluorophenyl)oxazole (2n). Synthesized from (*E*)-4-(*tert*-butyl)-*N*-(4-fluorostyryl)benzamide (**1n**) (297 mg); EtOAc/hexanes = 1:10; 230 mg, 78%; off-white solid. Mp: 76−77 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.8 Hz, 2H), 7.62 (dd, $^3J_{HH}$ = 9.6 Hz, $^4J_{HF}$ = 5.2 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.33 (s, 1H), 7.08 (dd, $^3J_{HH}$ = 8.8 Hz, $^3J_{HF}$ = 8.8 Hz, 2H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, $^1J_{CF}$ = 247.2 Hz), 161.3, 153.8, 150.1, 126.1, 125.9 (d, $^3J_{CF}$ = 8.1 Hz), 125.8, 124.6, 124.5 (*d*, $^4J_{CF}$ = 3.1 Hz), 123.0, 116.0 (d, $^2J_{CF}$ = 21.8 Hz), 34.9, 31.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.7. IR (neat cm^{-1}) 2951, 1499, 1227, 1140, 951, 827, 750, 708, 615. Anal. Calcd for $C_{19}H_{18}FNO$: C, 77.27; H, 6.14. Found: C, 77.29; H, 6.14.

5-(3,4-Difluorophenyl)-2-(3,4,5-trimethoxyphenyl)oxazole (2o). Synthesized from (*E*)-*N*-(3,4-difluorostyryl)-3,4,5-trimethoxybenzamide (**1o**) (349 mg). EtOAc/hexanes = 1:2, then 1:1; 310 mg, 90%; white solid. Mp: 145−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54−7.50 (m, 1H), 7.46−7.42 (m, 1H), 7.39 (s, 1H), 7.32 (s, 2H), 7.28−7.22 (m, 1H), 3.98 (s, 6H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.6, 150.8 (dd, $^1J_{CF}$ = 244.6 Hz, $^2J_{CF}$ = 10.2 Hz), 150.3 (dd, $^1J_{CF}$ = 248.4 Hz, $^2J_{CF}$ = 10.1 Hz), 149.3, 140.4, 125.1 (dd, $^3J_{CF}$ = 6.5 Hz, $^4J_{CF}$ = 4.1 Hz), 124.0, 122.4, 120.5 (dd, $^3J_{CF}$ = 6.3 Hz, $^4J_{CF}$ = 4.0 Hz), 118.2 (d, $^2J_{CF}$ = 17.9 Hz), 113.4 (d, $^2J_{CF}$ = 19.2 Hz), 103.6, 61.0, 56.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ −136.9, −137.4. IR (neat cm^{-1}) 2945, 2838, 1592, 1506, 1496, 1457, 1416, 1354, 1272, 1235, 1181, 1129, 1001, 841, 773, 728. Anal. Calcd for $C_{18}H_{15}F_2NO_4$: C, 62.25; H, 4.35. Found: C, 62.44; H, 4.35.

2,5-Di-*o*-tolyloxazole (2p). Synthesized from (*E*)-2-methyl-*N*-(2-methylstyryl)benzamide (**1p**) (251 mg); EtOAc/hexanes = 1:12, then 1:10; 199 mg, 80%; white solid. Mp: 77−79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.38 (s, 1H), 7.37−7.28 (ovrlp, 6H). 2.76 (s, 3H), 2.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 150.4, 137.4, 134.9, 131.8, 131.3, 130.1, 128.9, 128.4, 127.5, 126.9, 126.5, 126.4, 126.2, 126.1, 22.3, 22.1. IR (neat cm^{-1}) 2956, 2921, 1489, 1451, 1152, 1127, 1053, 774, 758, 724, 714. Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06. Found: C, 81.94; H, 6.09.

2-(Naphthalen-2-yl)-5-(*o*-tolyl)oxazole (2q). Synthesized from (*E*)-*N*-(2-methylstyryl)-2-naphthamide (**1q**) (287 mg); EtOAc/hexanes = 1:15, then 1:10; 221 mg, 78%; off-white solid. Mp: 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.84−7.71 (ovrlp, 4H), 7.42−7.40 (ovrlp, 2H), 7.29 (s, 1H), 7.27−7.23 (m, 1H), 7.18−1.17 (ovrlp, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 150.7, 134.6, 134.0, 132.9, 131.2, 128.6, 128.5, 128.2, 127.8, 127.11, 127.06, 126.61, 126.57, 126.3, 126.1, 126.0, 124.5, 123.1, 22.0. IR (neat cm^{-1}) 3057, 2953, 1721, 1463, 1375, 1277, 1195, 1130, 942, 859, 818, 752, 473. HRMS (ESI) calcd for $C_{20}H_{15}NO$ [M+H]: 286.1226; found 286.1231.

(*E*)-5-Phenyl-2-styryloxazole (4a).[13] Synthesized from *N*-((*E*)-styryl)cinnamamide (**3a**) (249 mg); EtOAc/hexanes = 1:12; 138 mg, 56%; off-white solid. Mp: 98−100 °C (lit.: 97−100 °C).[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 7.2 Hz, 2H), 7.59−7.55 (ovrlp, 3H), 7.46−7.32 (ovrlp, 7H), 6.99 (d, J = 16.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 151.0, 135.9, 135.7, 129.3, 129.1, 129.0, 128.6, 128.1, 127.3, 124.3, 123.9, 114.0. IR (neat cm^{-1}) 1520, 1480, 1133, 971, 942, 830, 753, 688. Anal. Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30. Found: C, 82.19; H, 5.16.

(*E*)-2-Phenyl-5-styryloxazole (4b).[42] Synthesized from *N*-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)benzamide (**3b**) (249 mg), with $CuBr_2$ (33.5 mg, 15 mol %) and pyridine (48 μL, 60 mol %); EtOAc/hexanes = 1:14; 99 mg, 40%; off-white solid. Mp: 81−82 °C (lit.: 82 °C).[42] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.6 Hz, 2H), 7.49−7.44 (ovrlp, 5H), 7.35 (t, J = 7.2 Hz, 2H), 7.27 (t, J = 7.2 Hz, 1H), 7.13 (t, J = 7.6 Hz, 2H), 6.90 (d, J = 16.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 150.4, 136.4, 130.5, 129.5, 128.9, 128.3, 127.4, 126.62, 126.57, 126.4, 113.1. IR (neat cm^{-1}) 1478, 1447, 1128, 961, 752, 824, 707, 693, 682. Anal. Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30. Found: C, 82.28; H 5.46.

(*E*)-2-(3,4-Dimethoxystyryl)-5-(4-methoxyphenyl)oxazole (Annuloline) (4c).[38] Synthesized from (*E*)-3-(3,4-dimethoxyphenyl)-*N*-((*E*)-4-methoxystyryl)acrylamide (**3c**) (339 mg), with $CuBr_2$ (33.5 mg, 15 mol %) and ethyl nicotinate (41.0 μL, 30 mol %). EtOAc/hexanes = 1:4, then 1:2. A yellow oily product was obtained, then recrystallized from CH_2Cl_2/hexanes (~1:2) by slow evaporation with the aid of a rotary evaporator; 192 mg, 57%; yellow solid. Mp: 104−106 °C (lit.: 104−107 °C).[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 16.4 Hz 1H), 7.27 (s, 1H), 7.11−7.08 (ovrlp, 2H), 6.95 (d, J = 8.4 Hz, 2H), 6.88−6.82 (ovrlp, 2H), 3.93 (s, 3H), 3.90 (s, 3H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 159.7, 150.6, 150.0, 149.2, 135.0, 128.7, 125.6, 122.1, 121.1, 120.8, 114.3, 112.0, 111.1, 108.8, 55.9, 55.8, 55.3. IR (neat cm^{-1}) 1599, 1518, 1444, 1263, 1233, 1131, 1021, 972, 823, 800, 768, 613.

5-Octyl-2-phenyloxazole (4d). Synthesized from (*E*)-*N*-(dec-1-en-1-yl)benzamide (**3d**) (259 mg); EtOAc/hexanes = 1:15; 107 mg, 42%; pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.2 Hz, 2H), 7.44−7.37 (ovrlp, 3H), 6.83 (s, 1H), 2.69 (t, J = 7.6 Hz, 2H), 1.68 (qu, J = 7.2 Hz, 2H), 1.38−1.27 (ovrlp, 10H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 153.3, 129.9, 128.7, 127.9, 126.0, 123.6, 31.9, 29.31, 29.25, 29.2, 27.7, 25.7, 22.7, 14.2. IR (neat, cm^{-1}) 2928, 2856, 1597, 1551, 1490, 1449, 1354, 1123, 1066, 1025, 982, 825, 775, 711, 691. Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01. Found: C, 79.32; H, 9.11.

2-(*tert*-Butyl)-5-phenyloxazole (4e).[9d] Synthesized from (*E*)-*N*-styrylpivalamide (**3e**) (203 mg), with $CuBr_2$ (33.5 mg, 15 mol %) and ethyl nicotinate (41.0 μL, 30 mol %); EtOAc/hexanes = 1:10; 121 mg, 60%; pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 2H), 7.38 (t, J = 7.6 Hz, 2H), 7.27 (t, J = 7.6 Hz, 1H), 7.20 (s, 1H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 150.6, 128.8, 128.4, 128.0, 124.0, 121.5, 33.8, 28.6. IR (neat cm^{-1}) 2971, 1549, 1447, 1367, 1244, 1145, 1121, 1060, 961, 822, 762, 747, 688. Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51. Found: C, 77.34; H, 7.71.

2-Cyclohexyl-5-phenyloxazole (4f) and 2-(1-Cyclohexenyl)-5-phenyloxazole (4f′) (10: 1). Synthesized from (*E*)-*N*-styrylcyclohexanecarboxamide (**3f**) (229 mg), with $CuBr_2$ (33.5 mg, 15 mol %) and ethyl nicotinate (41 μL, 30 mol %); EtOAc/hexanes = 1:20. **4f** and **4f′** were isolated as an inseparable, white product mixture (142 mg). The formation of **4f′** was further confirmed by GC−MS analysis ($[M]^+$ of **4f**: 227; $[M]^+$ of **4f′**: 225). The isolated yields of **4f** and **4f′** were estimated to be 54% (123 mg, 0.54 mmol) and 6% (14 mg, 0.06 mmol), respectively, by comparing the ratio of the proton signals of **4f** and **4f′** by ^{1}H NMR spectroscopy. The product mixture was recrystallized from CH_2Cl_2/acetonitrile (~2:1) by slow evaporation with the aid of a rotary evaporator to afford a pure **4f** as a white solid. ^{1}H NMR of an inseparable mixture of **4f** and **4f′** (400 MHz, $CDCl_3$) δ 7.63−7.58 (ovrlp, 2.2 H), 7.39−7.35 (ovrlp, 2.2 H), 7.30−7.25 (ovrlp, 1.1 H), 7.21 (ovrlp, 1.1 H), 6.85 (br, 0.1 H), 2.83 (tt, ^3J = 11.2 Hz, ^3J = 3.6 Hz, 1H), 2.52 (br, 0.2 H), 2.25 (br, 0.2 H), 2.13−2.10 (m, 2H), 1.85−1.81 (m, 2H), 1.76−1.59 (ovrlp, 3.2H), 1.44−1.25 (ovrlp, 3.2H). ^{13}C NMR of an inseparable mixture of **4f** and **4f′** (100 MHz, $CDCl_3$) (1) **4f**: δ 167.8, 150.5, 128.8, 128.4, 128.0, 123.9, 121.6, 37.6, 30.6, 25.8, 25.6. (2) **4f′**: δ 162.4, 150.1, 131.4, 128.3, 128.1, 126.1, 124.0, 122.8, 25.5, 24.5, 22.1, 21.8. Mp of pure **4f**: 88−90 °C. ^{1}H NMR of pure **4f** (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.8 Hz, 2H), 7.40 (t, J = 7.6 Hz, 2H), 7.29 (t, J = 7.6 Hz, 1H), 7.21 (s, 1H), 2.86 (tt, ^3J = 11.2 Hz, ^3J = 3.6 Hz, 1H), 2.15−2.11 (m, 2H), 1.87−1.82 (m, 2H), 1.75−1.60 (ovrlp, 3H), 1.46−1.26 (ovrlp, 3H). ^{13}C NMR of pure **4f** (100 MHz, $CDCl_3$) δ 168.0, 150.6, 128.9, 128.5, 128.1, 124.1, 121.7, 37.7, 30.8, 25.9, 25.8. IR of pure **4f** (neat cm^{-1}) 2922, 2854, 1551, 1448, 1117, 895, 835, 757, 705, 689. Anal. Calcd for $C_{15}H_{17}NO$ (**4f**): C, 79.26; H, 7.54. Found: C, 78.94; H, 7.57.

2-Phenyl-5-(thiophen-3-yl)oxazole (4g).[8f] Synthesized from (*E*)-*N*-(2-(thiophen-3-yl)vinyl)benzamide (**3g**) (229 mg), with $CuBr_2$ (33.5 mg, 15 mol %) and ethyl nicotinate (41 μL, 30 mol %); EtOAc/hexanes = 1:15, then 1:12; 134 mg, 59%; off-white solid. Mp: 73−74 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 2H), 7.56 (dd, J = 2.8 Hz, 1.2 Hz, 1H), 7.47−7.39 (ovrlp, 3H), 7.35 (dd, J = 5.2 Hz, 2.8 Hz, 1H), 7.32 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.26 (s,

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1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 148.1, 130.3, 129.2, 128.8, 127.4, 126.9, 126.2, 124.5, 123.0, 120.6. IR (neat cm^{-1}) 3107, 1611, 1500, 1447, 1396, 1130, 1066, 1022, 973, 849, 820, 772, 706, 689, 603. Anal. Calcd for $C_{13}H_9NOS$: C, 68.70; H, 3.99. Found: C, 68.46; H, 3.94.

5-Phenyl-2-(thiophen-3-yl)oxazole (4h).[43] Synthesized from (*E*)-*N*-styrylthiophene-3-carboxamide (**3h**) (229 mg); EtOAc/hexanes = 1:10; 171 mg, 75%; off-white solid. Mp: 71−72 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 2.8 Hz, 1.2 Hz, 1H), 7.65−7.63 (ovrlp, 3H), 7.40−7.33 (ovrlp, 4H), 7.38 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 150.5, 129.5, 128.9, 128.3, 127.9, 126.7, 125.9, 125.2, 124.1, 123.1. IR (neat cm^{-1}) 1592, 1493, 1132, 852, 787, 761, 717, 695.

5-Phenyl-2-(thiophen-2-yl)oxazole (4i).[38] Synthesized from (*E*)-*N*-styrylthiophene-2-carboxamide (**3i**) (229 mg); EtOAc/hexanes = 1:20, then 1:15; 106 mg, 47%; off-white solid. Mp: 63−65 °C (lit.: 59−61 °C).[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 4.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.41−7.37 (ovrlp, 3H), 7.36 (s, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.09 (t, J = 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 150.8, 130.0, 128.9, 128.4, 128.3, 128.0, 127.7, 127.6, 124.1, 123.3. IR (neat cm^{-1}) 3102, 1575, 1489, 1448, 1420, 1128, 1063, 945, 853, 823, 762, 718, 687.

2-(Furan-2-yl)-5-phenyloxazole (4j).[38] Synthesized from (*E*)-*N*-styrylfuran-2-carboxamide (**3j**) (211 mg); EtOAc/hexanes = 1:10; 110 mg, 53%; off-white solid. Mp: 66−67 °C (lit.: 61−63 °C).[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.6 Hz, 2H), 7.57−7.56 (m, 1H), 7.42−7.39 (ovrlp, 3H), 7.31 (t, J = 7.6 Hz, 1H), 7.06 (d, J = 3.2 Hz, 1H), 6.54 (dd, J = 3.2 Hz, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 150.9, 144.4, 143.0, 128.9, 128.6, 127.7, 124.2, 123.3, 111.9, 111.4. IR (neat cm^{-1}) 1519, 1452, 1171, 1135, 1008, 939, 895, 749, 720, 685, 643, 592.

Phenyl(5-(2-(thiophen-3-yl)oxazol-5-yl)-1*H*-indol-1-yl)-methanone (4k). Synthesized from (*E*)-*N*-(2-(1-benzoyl-1*H*-indol-5-yl)vinyl)thiophene-3-carboxamide (**3k**) (186 mg, 0.50 mmol, 1.0 equiv), $CuBr_2$ (8.4 mg, 0.038 mmol, 7.5 mol %), TBAB (193 mg, 0.60 mmol, 1.2 equiv), $K_2S_2O_8$ (176 mg, 0.65 mmol, 1.3 equiv), ethyl nicotinate (10.2 μL, 0.075 mmol, 15 mol %), and acetonitrile (5.0 mL, 0.1 M). EtOAc/hexanes = 1:5; 109 mg, 0.29 mmol, 59%; pale yellow solid. Mp: 148−149 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 8.8 Hz, 1H), 8.02 (dd, J = 3.2 Hz, 1.2 Hz, 1H), 7.95 (d, J = 1.2 Hz, 1H), 7.77−7.70 (ovrlp, 4H), 7.63 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.2 Hz, 2H), 7.43−7.41 (ovrlp, 2H), 7.35 (d, J = 3.6 Hz, 1H), 6.67 (d, J = 4.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 158.0, 151.0, 135.8, 134.2, 132.1, 131.2, 129.5, 129.3, 128.7, 126.7, 126.0, 125.1, 123.9, 122.6, 121.3, 116.9, 116.6, 108.6. IR (neat cm^{-1}) 1686, 1598, 1457, 1367, 1336, 1191, 877, 724, 713. Anal. Calcd for $C_{22}H_{14}N_2O_2S$: C, 71.33; H, 3.81. Found: C, 71.04; H, 3.97.

■ ASSOCIATED CONTENT

Supporting Information

All spectral data. 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.

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