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Palladium-Catalyzed Intramolecular Cyclization of Ynamides: Synthesis of 4-Halo-oxazolones

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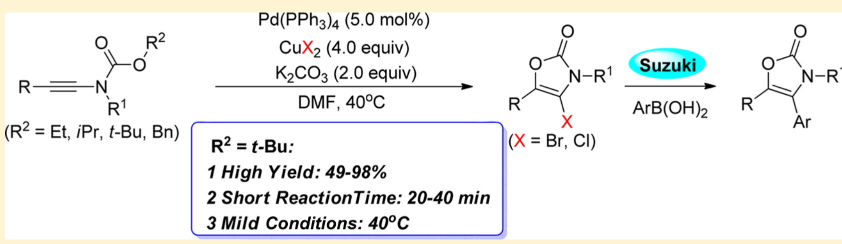
Supporting Information

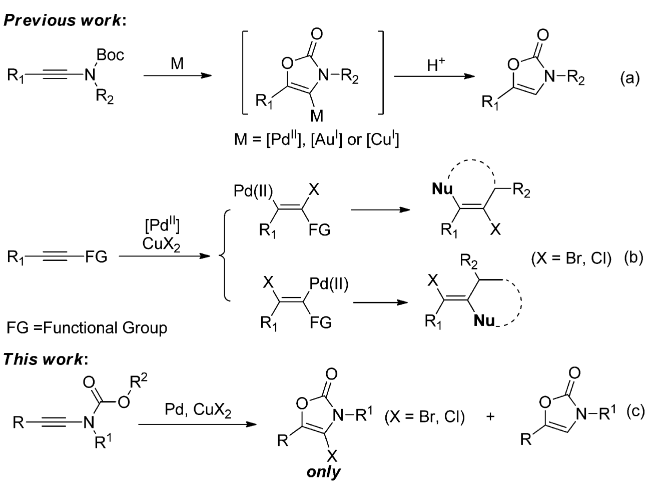


ABSTRACT: A mild and efficient methodology involving $Pd(PPh_3)_4$-catalyzed intramolecular cyclization of *N*-alkynyl alkyloxycarbamates with $CuCl_2$ or $CuBr_2$ for the synthesis of 4-halo-oxazolones was developed. This reaction exhibiting good functional tolerance provided a new, efficient, and rapid synthetic process to 4-halo-oxazolones. The resulting 4-halo-oxazolones can serve as great potential precursors for the 3,4,5-trisubstituted oxazolones via a Pd-catalyzed cross-coupling reaction.

INTRODUCTION

Oxazolones are not only valuable building blocks in organic synthesis but also a recurring functional group in a large number of natural products and bioactive compounds.[1] Therefore, great efforts have been directed toward developing synthetic approaches for the construction of this privileged structure,[2] among which the metal-catalyzed (e.g., Au, Pd, and Cu) cyclization of the *N*-alkynyl *tert*-butyloxycarbamates is considered to be one of the most effective strategies (Scheme 1, a).[3] For instance, Gagosz[3a] reported the Au-catalyzed cycloisomerization, which provided the efficient and rapid process for the synthesis of 3,5-disubstituted oxazolones. Despite these advances, the effective synthesis of 3,4,5-multisubstituted oxazolones and modification of the 4-position of oxazolones still remain highly challenging areas.[4]

Scheme 1. Pd-catalyzed Cyclization of the *N*-alkynyl alkyloxycarbamates



Meanwhile, the halopalladation of alkynes has been proven to be an extremely efficient and convenient method for the construction of important carbo- and heterocycles in organic synthesis.[5] First, the halopalladation of alkynes generates a versatile reactive σ-vinylpalladium intermediate. Such a σ-vinylpalladium intermediate could be next trapped by some nucleophilic groups leading to corresponding compounds (Scheme 1, b). In addition, after learning of the widespread application of the carbonyl oxygen as nucleophile in transition-metal-catalyzed reactions,[6] we conceived that during the process of halopalladation a carbamate group could be used as oxygen source to capture the σ-vinylpalladium intermediate. After pursuing our recent interest in the functionalization of ynamides,[7] we herein report a novel Pd-catalyzed cyclization of *N*-alkynyl alkyloxycarbamates to afford the corresponding 4-halo-oxazolones in good yields under mild conditions. Furthermore, this method affords oxazolones with a halogen (Cl or Br) at the 4-position, which provides an attractive and useful route to introduce new groups for the synthesis of new bioactive products (Scheme 1, c).[8]

RESULTS AND DISCUSSION

In the initial experiments, *tert*-butyl *N*-phenyl-*N*-(phenylethynyl)carbamate (**1a**) was used as a model substrate to screen the optimal reaction conditions. Compound **1a** and 3.0 equiv of $CuBr_2$ were treated with 10 mol % of $Pd(OAc)_2$ and 2.0 equiv of *t*-BuOK in DMA at 60 °C. To our delight, the

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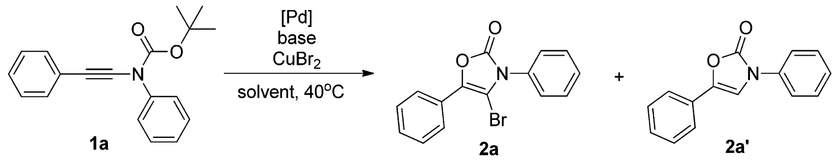
Table 1. Optimization of Reaction Conditions[a]



entry	[Pd]	base	$CuBr_2$ (equiv)	solvent	temp (°C)	**2a**/**2a′** yield[b] (%)
1	$Pd(OAc)_2$	*t*-BuOK	3.0	DMA	60	41/12
2	$Pd(OAc)_2$	Na_2CO_3	3.0	DMA	40	43/22
3	$Pd_2(dba)_3$	Na_2CO_3	3.0	DMA	40	42/17
4	$PdCl_2$	Na_2CO_3	3.0	DMA	40	32/16
5	$PdCl_2(PPh_3)_4$	Na_2CO_3	3.0	DMA	40	38/18
6	$Pd(PPh_3)_4$	Na_2CO_3	3.0	DMA	40	73/0
7[c]	$Pd(PPh_3)_4$	Na_2CO_3		DMA	40	NR
8[d]		Na_2CO_3	3.0	DMA	40	NR
9	$Pd(PPh_3)_4$	K_2CO_3	3.0	DMA	40	80/0
10	$Pd(PPh_3)_4$	$KHCO_3$	3.0	DMA	40	77/0
11	$Pd(PPh_3)_4$	K_3PO_4	3.0	DMA	40	70/0
12	$Pd(PPh_3)_4$	K_2CO_3	3.0	THF	40	65/0
13	$Pd(PPh_3)_4$	K_2CO_3	3.0	toluene	40	39/0
14	$Pd(PPh_3)_4$	K_2CO_3	3.0	DMSO	40	14/0
15	$Pd(PPh_3)_4$	K_2CO_3	3.0	DCM	40	38/0
16	$Pd(PPh_3)_4$	K_2CO_3	3.0	DMF	40	83/0
17	$Pd(PPh_3)_4$	K_2CO_3	2.0	DMF	40	52/0
18	$Pd(PPh_3)_4$	K_2CO_3	4.0	DMF	40	91/0
19[e]	$Pd(PPh_3)_4$	K_2CO_3	4.0	DMF	40	90/0

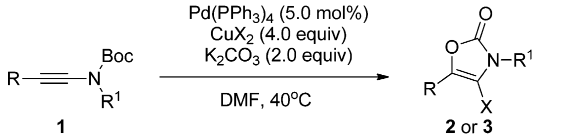
[a]The reaction was carried out with **1a** (0.30 mmol), Pd catalyst (10 mol %), base (0.6 mmol), and $CuBr_2$ in solvent (2.0 mL) under N_2 atmosphere for 20 min. NR = no reaction. [b]Yield was determined by ^1H NMR on the crude reaction mixture using 1,3,5-trimethylbenzene as an internal standard. [c]Compound **1a** (91%) was recovered. [d]Compound **1a** (83%) was recovered. [e]5.0 mol % catalyst loading.

desired 4-bromo-3,5-diphenyl-3*H*-oxazol-2-one **2a** was obtained in 41% yield along with nonhalo product 3,5-diphenyl-3*H*-oxazol-2-one **2a′** in 12% yield (Table 1, entry 1). Different Pd catalysts were applied. Interestingly, the single product **2a** was obtained in 73% yield when $Pd(PPh_3)_4$ was used as catalyst (Table 1, entries 2−6). A blank experiment indicated that no reaction occurred in the absence of the palladium catalyst (Table 1, entry 7). The reaction also failed without the addition of the copper salt (Table 1, entry 8). To further optimize the reaction, different bases were examined in which K_2CO_3 gave the best performance (Table 1, entries 9−11). Among the solvents screened, DMF was superior to DMA, THF, toluene, DMSO, and DCM (Table 1, entries 12−16). The employment of 4.0 equiv of $CuBr_2$ gave the highest yield (91%) of **2a** (Table 1, entry 18). A similar result was observed when 5.0 mol % of $Pd(PPh_3)_4$ was utilized in the reaction (Table 1, entry 19) (for more details, see the Supporting Information).

Under the optimized reaction conditions, we examined the scope and generality of various ynamides in this transformation (Table 2). Groups such as methyl and methoxy that are substituted in the aryl ring were tolerated and readily produced high yields of the corresponding 4-bromo-oxazolones (Table 2, entries 1−3). *tert*-Butyl *N*-phenyl-*N*-(naphthalen-2-ylethynyl)-carbamate **1d** also worked well, leading to 4-bromo-5-(naphthalen-2-yl)-3-phenyl-3*H*-oxazol-2-one **2d** in 68% yield (Table 2, entry 4). Ynamides with electron-withdrawing groups on the *meta*-positions of the *N*-aryl ring, such as F, Cl, Br, and CF_3, generated the corresponding 4-bromo-oxazolones in 73−90% yields (Table 2, entries 5−8). On the other hand, ynamides with electron-donating groups, such as Me and MeO on the *meta*-positions of their *N*-aryl rings, gave the desired products in 91−94% yields (Table 2, entries 9 and 10). Meanwhile, the *ortho*-effect was not obvious for methyl and bromo groups on the *ortho*-positions of the *N*-aryl ring in the reactions (Table 2, entries 11 and 12). Ynamide with methyl on the *para*-positions the *N*-aryl ring was also tolerated, leading to the desired product in 83% yield (Table 2, entry 13). However, ynamide with bromo on the *para*-positions of the *N*-aryl ring gave a lower yield compared with either the *meta*- or *ortho*-substituted product (Table 2, entry 14). Under the recommended reaction conditions, substrates possessing a 2-naphthyl group on the nitrogen atom (Table 2, entry 15) furnished the desired product in good yield. Furthermore, ynamides with a *N*-benzyl or *N*-butyl group also successfully produced the desired 4-bromo-oxazolones in moderate yields (Table 2, entries 16 and 17). Alkyl-substituted ynamides could also have moderate yield successfully under the reaction conditions, and the yield probably was not affected by the length of the alkyl chain (Table 2, entries 18 and 19). Finally, the reaction of vinyl alkynyl-substituted substrate (*E*)-*tert*-butyl (2-bromophenyl)(4-phenylbut-3-en-1-yn-1-yl)carbamate (**1t**) with $CuBr_2$ gave a good yield (Table 2, entry 20). The structures of **2a** and **2m** were further confirmed via single-crystal X-ray diffraction (for more details, see the Supporting Information).

We also tested the Pd-catalyzed cyclizations of *N*-alkynyl *tert*-butyloxycarbamates **1** in the presence of $CuCl_2$ (Table 2, entries 21−26). These reactions proceeded well to afford chloro-containing oxazolones **3** in moderate to good yields. For example, a 74% yield of product **3a** was obtained when **1a** was employed in a reaction with $CuCl_2$. Moreover, under the optimized reaction conditions, various substrates bearing groups on the *ortho*-, *meta*-, and *para*-positions of the *N*-aryl ring were converted (moderate to high yields) into the

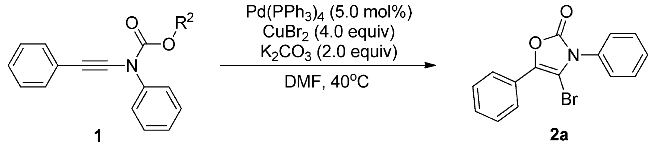
Table 2. Pd-Catalyzed Formation of 4-Bromo-oxazolones[a]



entry	R	R[1]	X	product	isolated yield (%)
1	Ph (**1a**)	Ph	Br	**2a**	84
2	*p*-MePh (**1b**)			**2b**	93
3	*p*-MeOPh (**1c**)			**2c**	85
4[b]	2-naphthyl (**1d**)			**2d**	68
5	Ph	*m*-FPh (**1e**)	Br	**2e**	73
6		*m*-ClPh (**1f**)		**2f**	87
7		*m*-BrPh (**1g**)		**2g**	90
8		*m*-CF_3Ph (**1h**)		**2h**	83
9		*m*-MePh (**1i**)		**2i**	94
10		*m*-MeOPh (**1j**)		**2j**	91
11		*o*-MePh (**1k**)		**2k**	94
12		*o*-BrPh (**1l**)		**2l**	98
13		*p*-MePh (**1m**)		**2m**	83
14		*p*-BrPh (**1n**)		**2n**	64
15[b]		2-naphthyl (**1o**)		**2o**	74
16		Bn (**1p**)		**2p**	51
17		*n*-C_4H_9 (**1q**)		**2q**	53
18	*n*-C_4H_9 (**1r**)	Ph	**Br**	**2r**	54
19	*n*-C_8H_{17} (**1s**)			**2s**	49
20	(*E*)-styryl (**1t**)	*o*-BrPh	Br	**2t**	71
21[c]	Ph	Ph (**1a**)	Cl	**3a**	74
22[c]		*m*-BrPh (**1g**)		**3g**	84
23[c]		*m*-MeOPh (**1j**)		**3j**	88
24[c]		*o*-BrPh (**1l**)		**3l**	87
25[c]		*p*-BrPh (**1n**)		**3n**	65
26[c]		Bn (**1p**)		**3p**	81

[a]Reaction conditions: **1** (0.3 mmol), $Pd(PPh_3)_4$ (5.0 mol %), CuX_2 (4.0 equiv), and K_2CO_3 (0.6 mmol) in DMF (2.0 mL) at 40 °C for 20 min. [b]Reaction time was 30 min. [c]Reaction time was 40 min.

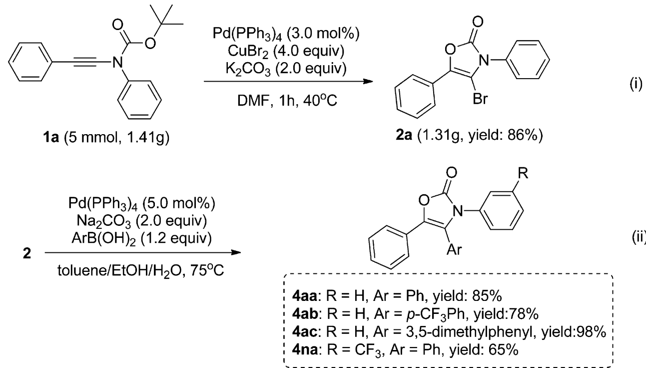
Table 3. Cyclizations of Ynamides Containing Various Leaving Groups[a]



entry	R[2]	time	yield of **2a**[b] (%)	recovery of **1**[b] (%)
1	Et (**1u**)	20 h	30	33
2	*i*-Pr (**1v**)	20 h	34	39
3	*t*-Bu (**1a**)	20 min	90	0
4	Bn (**1w**)	20 min	65	0

[a]Reaction conditions: **1** (0.3 mmol), $Pd(PPh_3)_4$ (5.0 mol %), $CuBr_2$ (4.0 equiv), and K_2CO_3 (0.6 mmol) in DMF (2.0 mL) at 40 °C. [b]It was determined by ^{1}H NMR on the crude reaction mixture using 1,3,5-trimethylbenzene as an internal standard.

Scheme 2. Scale-up Experiment and Suzuki−Miyaura Coupling



corresponding 4-chloro-oxazolones. Ynamides in general give a relatively poor or similar yield in the presence of $CuCl_2$ compared with the $CuBr_2$ conditions (Table 2, entries 21−25); interestingly, *tert*-butyl *N*-benzyl-*N*-(phenylethynyl)-carbamate (**1p**) took part in the reaction readily and was transformed to the corresponding product in 81% yield.

In Table 3, we then studied the effect of varying leaving groups (e.g., Et, *i*-Pr, *t*-Bu, Bn) on the ester moiety. For ynamides containing leaving groups, such as Et and *i*-Pr, cyclization took place in poor yields. As reported,[9] *N*-carbobenzyloxy (*N*-Cbz)-protected amines were great potential structures for the synthesis of cyclic carbamates, and *N*-Cbz-protected ynamide (**1w**) exhibited good reactivity to afford **2a** in satisfying yield.

To demonstrate the synthetic potential of this strategy, **1a** (1.41 g, 5 mmol) was allowed to react under the optimized conditions. This reaction could be scaled up to 5 mmol in a high yield, and the Pd catalyst loading could be reduced to 3% mol with comparable efficiency (Scheme 2). We then attempted to introduce more groups into the oxazolone scaffold via Pd-catalyzed cross-coupling reactions. Thus, the Suzuki−Miyaura coupling reaction was investigated (Scheme 2, (i)). Product **2** easily underwent a Suzuki-coupling reaction by treatment with arylboronic acids under toluene/EtOH/H_2O conditions using $Pd(PPh_3)_4$ as the Pd catalyst (Scheme 2, (ii)).

To understand the mechanism of the reaction, control experiments were conducted (Scheme 3). Compound **1a** could not produce 4-chloro-3,5-diphenyl-3*H*-oxazol-2-one **3a** in the absence of $CuCl_2$ using 1.0 equiv of $PdCl_2(PPh_3)_2$ as chlorine source, which revealed that C−X formation does not originate from the cleavage of the C−Pd bond.[10] In contrast, the desired product was obtained in 41% yield in the presence of $CuCl_2$. It is noteworthy that **1a** also failed to produce the corresponding oxazolone **3a** using the $Pd(PPh_3)_4$/CuCl system instead of the $Pd(PPh_3)_4/CuCl_2$ system. These results revealed the important role of CuX_2 in this cyclization system. Furthermore, the non-halo product 3,5-diphenyl-3*H*-oxazol-2-one **2a′** could not produce **3a** under the recommended reaction conditions, which suggested that the formation of C−X bond might be followed by the intramolecular cyclization.

According to the experimental results and the reported literature, a proposed mechanism for this $Pd(PPh_3)_4$-catalyzed intramolecular cyclization of *N*-alkynyl alkyloxycarbamates is shown in Scheme 4. Pd(0) was first converted to Pd(II) species in this reaction system.[11] The activation of the triple bond in *N*-alkynyl alkyloxycarbamates **1** with Pd(II) produces the intermediate **A.**[12] Nucleophilic attack of the bromo or chloro anion generates *σ*-vinylpalladium intermediate **B**,[5e,11a,13] which transforms into the oxopalladium complex **C** coordinating with base.[14] The resulting oxopalladium intermediate **C** has been suggested to undergo the reductive elimination to form the corresponding 4-halo-oxazolones and the Pd(0) species.[15]

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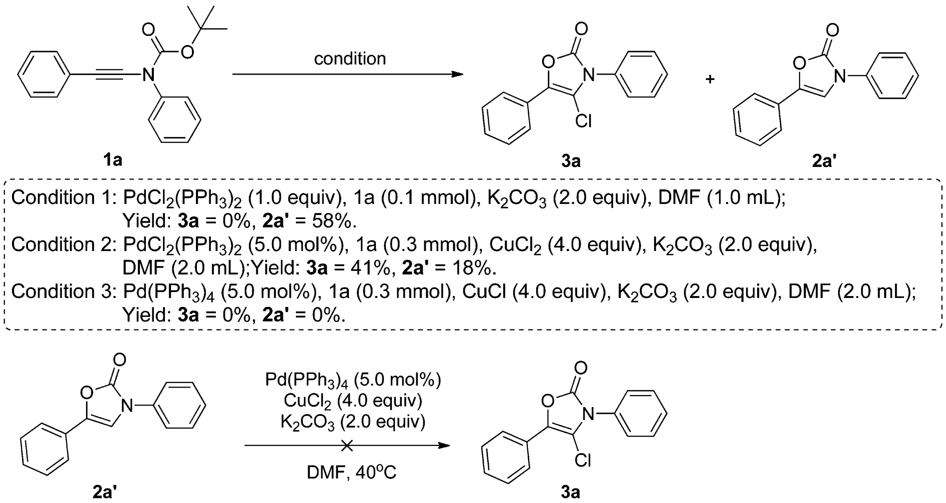
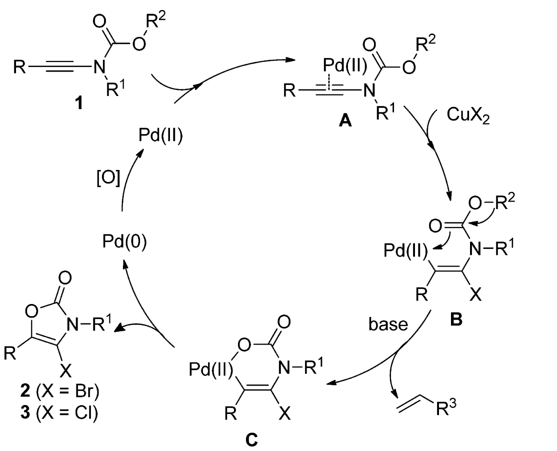
Scheme 3. Experiment for Mechanistic Study



Scheme 4. Proposed Mechanism for this Cyclization



■ CONCLUSIONS

In summary, we have developed a novel and efficient protocol for the synthesis of 4-halo-oxazolones by the halopalladation and carbon−oxygen-forming process. In the presence of $Pd(PPh_3)_4$ and CuX_2 (X = Cl or Br), a variety of *N*-alkynyl alkyloxycarbamates underwent the reaction to afford 4-halo-oxazolones in moderate to excellent yields. Moreover, a halogen at the 4-position of these products provides an attractive and useful route to introduce new groups for the synthesis of new bioactive products. Further studies on transition-metal-catalyzed C−C, C−N, and C−O bond formation of ynamides are being conducted in our laboratory and will be reported in due course.

■ EXPERIMENTAL SECTION

General Methods. All reactions were performed in reaction tubes under nitrogen atmosphere. ^{1}H NMR and ^{13}C NMR were recorded at, respectively, 400 and 100 MHz using $CDCl_3$ as solvent. The following abbreviations are used to describe peak patterns where appropriate: b =broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants are reported in hertz (Hz). Chemical shifts are reported in ppm relative to the internal standard tetramethylsilane (δ = 0 ppm) for ^{1}H NMR and deuteriochloroform (δ = 77.00 ppm) for ^{13}C NMR. High-resolution mass spectra (HRMS) were recorded on an ESI-TOF (time-of-flight) mass spectrometer. Melting points were measured with a micro melting point apparatus.

Ynamide Synthesis: Typical Procedure I. Compounds were synthesized according to a literature procedure.[3a] To a mixture of carbamates (8.0 mmol), K_3PO_4 (16 mmol), $CuSO_4{\cdot}5H_2O$ (0.8 mmol), and 1,10-phenanthroline (1.6 mmol) in a reaction vial was added a solution of bromoalkyne[16] (8.8 mmol) in toluene (15 mL). The reaction mixture was capped and heated in an oil bath at 85 °C for 18 h while being monitored by TLC. Upon completion, the reaction mixture was cooled to room temperature, diluted with EtOAc, and filtered through Celite, and the filtrate was concentrated in vacuum. The crude products were purified by silica gel flash chromatography on a silica gel column with petroleum ether (PE) and ethyl acetate (EA) as eluent to afford directing products.

*tert-Butyl N-(phenylethynyl)-N-(p-tolyl)carbamate (**1b**):* yield 68% (1.66 g); white solid; mp 71−72 °C (*n*-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 50:1); ^{1}H NMR δ 7.55−7.50 (m, 2 H), 7.42−7.35 (m, 2 H), 7.30 (d, J = 8.4 Hz, 2 H), 7.27−7.22 (m, 1 H), 7.10 (d, J = 8.0 Hz, 2 H), 2.33 (s, 3 H), 1.56 (s, 9H); ^{13}C NMR δ 153.0, 139.8, 137.4, 130.9, 129.0, 128.7, 126.5, 124.6, 120.2, 83.4, 82.9, 70.0, 28.0, 21.4; IR ν (KBr, cm^{-1}) 2991, 1732, 1643, 1617, 1491, 1397, 1364, 1287, 1254, 1150, 1004, 820, 769; MS (ESI) m/z 330.0(100) [M + Na]$^+$. Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.06; H, 7.34; N, 4.61.

*tert-Butyl N-((4-methoxyphenyl)ethynyl)-N-(phenyl)carbamate (**1c**):* yield 67% (1.73 g); yellow oil; R_f 0.20 (ν_{PE}/ν_{EA} = 50:1); ^{1}H NMR δ 7.44 (dd, J_1 = 1.2 Hz, J_2 = 8.8 Hz, 2 H), 7.32−7.24 (m, 4 H), 7.15 (t, J = 7.6 Hz, 1 H), 6.74 (d, J = 8.8 Hz, 2 H), 3.69 (s, 3 H), 1.47 (s, 9H); ^{13}C NMR δ 158.0, 152.0, 138.8, 131.6, 127.7, 125.4, 123.6, 114.2, 112.8, 82.3, 81.1, 68.6, 54.2, 26.9; IR ν (KBr, cm^{-1}) 2977, 1731, 1602, 1511, 1364, 1288, 1249, 1155, 1031, 831, 762; MS (ESI) m/z 346.1(100) [M + Na]$^+$; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{21}NO_3$ [M + Na]$^+$ 346.1403, found 346.1409.

*tert-Butyl N-(naphthalen-2-ylethynyl)-N-(phenyl)carbamate (**1d**):* yield 45% (1.21 g); yellow oil; R_f 0.20 (ν_{PE}/ν_{EA} = 40:1); ^{1}H NMR δ 7.82 (s, 1 H), 7.72−7.65 (m, 3 H), 7.51−7.46 (m, 2 H), 7.41−7.31 (m, 5 H), 7.23−7.17 (m, 1 H), 1.51 (s, 9H); ^{13}C NMR δ 151.9, 138.6, 132.1, 131.3, 129.1, 127.8, 127.1, 126.8, 126.7, 126.5, 125.7, 125.4, 125.2, 123.7, 119.7, 82.6, 69.5, 27.0; IR ν (KBr, cm^{-1}) 1770, 1623, 1497, 1378, 1228, 1173, 1056, 1008, 977, 750, 694; MS (ESI) m/z 366.2 (100) [M + Na]$^+$; HRMS (ESI-TOF) m/z calcd for $C_{23}H_{21}NO_2$ [M + Na]$^+$ 366.1470, found 366.1482.

*tert-Butyl N-(3-methoxyphenyl)-N-(phenylethynyl)carbamate (**1j**):* yield 74% (1.88 g); white solid; mp 57−58 °C (*n*-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 50:1); ^{1}H NMR δ 7.42−7.37 (m, 2 H), 7.32−7.29 (m, 4 H), 7.16−7.09 (m, 2 H), 6.81 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1 H), 3.82 (s, 3 H), 1.57 (s, 9H); ^{13}C NMR δ 159.9, 152.8, 140.7, 130.8, 129.4, 128.2, 127.4, 123.4, 117.0, 112.3, 110.6, 83.5, 70.3, 55.4, 28.0; IR ν (KBr, cm^{-1}) 2977, 2934, 1731, 1602, 1511, 1364, 1288. 1249, 1155, 1031, 831, 762; MS (ESI) m/z 346.1 (100) [M +

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Na]$^+$. Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.36; H, 6.80; N, 4.17.

Ethyl N-phenyl-N-(phenyl-ethynyl)carbamate (1u):[17] yield 76% (1.62 g); yellow oil; R_f 0.20 (ν_{PE}/ν_{EA} = 20:1); ^{1}H NMR δ 7.57−7.52 (m, 2 H), 7.45−7.38 (m, 4 H), 7.33−7.25 (m, 4 H), 4.35 (q, J = 7.2 Hz, 2 H), 1.38 (t, J = 7.2 Hz, 3 H); ^{13}C NMR δ 154.3, 139.5, 131.2, 128.9, 128.2, 127.7, 126.9, 124.6, 123.0, 83.0, 70.1, 63.7, 14.3.

Isopropyl N-phenyl-N-(phenylethynyl)carbamate (1v): yield 59% (1.30 g); yellow oil; R_f 0.20 (ν_{PE}/ν_{EA} = 20:1); ^{1}H NMR δ 7.57−7.52 (m, 2 H), 7.43−7.37 (m, 4 H), 7.33−7.26 (m, 4 H), 5.08 (m, 1 H), 1.37 (d, J = 6.4 Hz, 3 H); ^{13}C NMR δ 153.8, 139.6, 131.1, 128.9, 128.2, 127.5, 126.7, 124.6, 123.2, 83.2, 71.9, 70.1, 21.9; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{17}NO_2$ [M + Na]$^+$ 302.1157, found 302.1163.

Benzyl N-phenyl-N-(phenylethynyl)carbamate (1w): yield 29% (0.76 g); yellow oil; R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.57−7.53 (m, 2 H), 7.46−7.33 (m, 9 H), 7.32−7.26 (m, 4 H), 5.33 (s, 2 H); ^{13}C NMR δ 154.1, 139.4, 135.4, 131.2, 129.0, 128.6, 128.3, 128.2, 127.9, 127.7, 127.0, 124.6, 122.9, 82.8, 70.4, 68.9; HRMS (ESI-TOF) m/z calcd for $C_{22}H_{17}NO_2$ [M + Na]$^+$ 350.1157, found 350.1169.

General Procedure for Pd-Catalyzed Synthesis of 4-Halo-oxazolones in the Presence of CuX_2: Typical Procedure II. Ynamides **1** (0.3 mmol), $Pd(PPh_3)_4$ (0.015 mmol), CuX_2 (1.2 mmol), K_2CO_3 (0.6 mmol), and DMF (2.0 mL) were placed into a 10 mL Schlenk tube, and then the temperature was increased to 40 °C. The solution was stirred under an N_2 atmosphere for 20 min and monitored by TLC. After being cooled to room temperature, the reaction mixture was quenched with ethyl acetate (15 mL) and washed with water (30 mL). The aqueous phase was extracted twice with EtOAc (3 × 10 mL), and the combined organic layer was dried over anhydrous Na_2SO_4. After evaporation of the solvents under vacuum, the crude products were purified by flash chromatography on a silica gel column with petroleum ether (PE) and ethyl acetate (EA) as the eluent to afford the desired product.

4-Bromo-3,5-diphenyl-3H-oxazol-2-one (2a): yield 84% (80.3 mg); white solid; mp 160−161 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.88−7.83 (m, 2 H), 7.56−7.35 (m, 8 H); ^{13}C NMR δ 152.1, 136.7, 132.8, 129.4, 129.2, 128.8, 128.7, 127.7, 126.5, 124.9, 97.7; IR ν (KBr, cm^{-1}) 3062, 1745, 1498, 1379, 1223, 1058, 966, 756, 690; MS (ESI) m/z 338.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{15}H_{10}BrNO_2$: C, 56.99; H, 3.19; N, 4.43. Found: C, 57.00; H, 3.32; N, 4.15.

3,5-Diphenyl-3H-oxazol-2-one (2a′):[1] ^{1}H NMR δ 7.62 (d, J = 7.6 Hz, 2 H), 7.56 (d, J = 7.2 Hz, 2 H), 7.47 (t, J = 7.6 Hz, 2 H), 7.42 (t, J = 7.2 Hz, 2 H), 7.36−7.28 (m, 2 H), 7.17 (s, 1 H); ^{13}C NMR δ 152.6, 139.9, 135.5, 129.5, 128.9, 128.6, 127.0, 126.6, 123.2, 121.0, 108.4;

4-Bromo-3-phenyl-5-(p-tolyl)-3H-oxazol-2-one (2b): yield 93% (91.8 mg); white solid; mp 170−171 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.74 (d, J = 8.4 Hz, 2 H), 7.56−7.38 (m, 5 H), 7.26 (d, J = 8.4 Hz, 2 H), 2.39 (s, 3 H); ^{13}C NMR δ 152.2, 139.0, 137.0, 132.9, 129.39, 129.37, 129.1, 127.7, 124.9, 123.7, 96.9, 21.4; IR ν (KBr, cm^{-1}) 3056, 1763, 1621, 1496, 1376, 1229, 1060, 1008, 966, 813, 696; MS (ESI) m/z 352.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}BrNO_2$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.16; H, 3.76; N, 4.03.

4-Bromo-5-(4-methoxyphenyl)-3-phenyl-3H-oxazol-2-one (2c): yield 85% (88.6 mg); white solid; mp 159−160 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.79 (d, J = 9.2 Hz, 2 H), 7.55−7.44 (m, 3 H), 7.43−7.38 (m, 2 H), 6.98 (d, J = 9.2 Hz, 2 H), 3.86 (s, 3 H); ^{13}C NMR δ 160.0, 152.2, 136.9, 133.0, 129.4, 129.1, 127.7, 126.6, 119.1, 114.2, 95.9, 55.4; IR ν (KBr, cm^{-1}) 3066, 1774, 1598, 1504, 1369, 1254, 1220, 1177, 1063, 1018, 964, 862, 701; MS (ESI) m/z 368.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}BrNO_3$: C, 55.51; H, 3.49; N, 4.05. Found: C, 55.67; H, 3.60; N, 3.80.

4-Bromo-5-(naphthalen-2-yl)-3-phenyl-3H-oxazol-2-one (2d): yield 68% (74.0 mg); white solid; mp 178−180 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 10:1); ^{1}H NMR δ 8.32 (s, 1 H), 7.99 (dd, J_1= 1.6 Hz, J_2 = 8.4 Hz, 1 H), 7.92−7.82 (m, 3 H), 7.57−7.42 (m, 7 H); ^{13}C NMR δ 152.2, 136.9, 133.0, 132.9, 132.8, 129.4, 129.3, 128.5, 128.4, 127.8, 127.7, 126.9, 126.8, 124.6, 123.8, 122.0, 98.1; IR ν (KBr, cm^{-1}) 1737, 1690, 1617, 1530, 1496, 1395, 1302, 1251, 1152, 818, 747; MS (ESI) m/z 388.1 (100) [M + Na]$^+$. Anal. Calcd for $C_{19}H_{12}BrNO_2$: C, 62.32; H, 3.30; N, 3.82. Found: C, 62.41; H, 3.47; N, 3.57.

4-Bromo-3-(3-fluorophenyl)-5-phenyl-3H-oxazol-2-one (2e): yield 73% (73.6 mg); white solid; mp 169−170 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.87−7.83 (m, 2 H), 7.55−7.35 (m, 4 H), 7.26−7.16 (m, 3 H); ^{13}C NMR δ 162.6 (d), 151.8, 137.1, 134.0 (d), 130.6 (d), 129.0, 128.8, 126.3, 125.0, 123.5 (d), 116.4 (d), 115.3 (d), 97.1; IR ν (KBr, cm^{-1}) 1749, 1638, 1615, 1389, 1237, 1063, 1021, 983, 760, 682; MS (ESI) m/z 356.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9BrFNO_2$: C, 53.92; H, 2.71; N, 4.19. Found: C, 53.92; H, 2.67; N, 4.08.

4-Bromo-3-(3-chlorophenyl)-5-phenyl-3H-oxazol-2-one (2f): yield 87% (91.8 mg); white solid; mp 156−157 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.85 (d, J = 7.6 Hz, 2 H), 7.50−7.43 (m, 5 H), 7.42−7.30 (m, 2 H); ^{13}C NMR δ 151.8, 137.1, 135.0, 133.8, 130.3, 129.5, 129.0, 128.8, 128.0, 126.3, 125.9, 125.0, 97.1; IR ν (KBr, cm^{-1}) 3077, 1747, 1640, 1591, 1483, 1380, 1226, 1060, 976, 757,691; MS (ESI) m/z 372.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9BrClNO_2$: C, 51.39; H, 2.59; N, 4.00. Found: C, 51.43; H, 2.53; N, 3.67.

4-Bromo-3-(3-bromophenyl)-5-phenyl-3H-oxazol-2-one (2g): yield 90% (109.7 mg); white solid; mp 142−143 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.85 (d, J = 7.2 Hz, 2 H), 7.63−7.59 (m, 2 H), 7.50−7.35 (m, 5 H); ^{13}C NMR δ 151.8, 137.1, 133.9, 132.4, 130.8, 130.6, 129.0, 128.8, 126.4, 126.2, 125.0, 122.7, 97.1; IR ν (KBr, cm^{-1}) 3059, 1750, 1658, 1595, 1501, 1397, 1214, 1133, 1052, 1023, 980, 733, 689; MS (ESI) m/z 416.0 (48) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9Br_2NO_2$: C, 45.61; H, 2.30; N, 3.55. Found: C, 45.75; H, 2.33; N, 3.38.

4-Bromo-5-phenyl-3-(3-(trifluoromethyl)phenyl)-3H-oxazol-2-one (2h): yield 83% (95.7 mg); white solid; mp 136−137 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.88−7.83 (m, 2 H), 7.76−7.62 (m, 4 H), 7.50−7.38 (m, 3 H); ^{13}C NMR δ 151.8, 137.4, 133.4, 132.1 (q), 131.0, 130.1, 129.2, 128.8, 126.2, 125.9 (q), 125.1, 124.8 (q), 122.0, 96.8; IR ν (KBr, cm^{-1}) 3065, 1756, 1641, 1453, 1392, 1324, 1179,1121,749, 687; MS (ESI) m/z 406.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_9BrF_3NO_2$: C, 50.03; H, 2.36; N, 3.65. Found: C, 50.22; H, 2.52; N, 3.25.

4-Bromo-5-phenyl-3-(m-tolyl)-3H-oxazol-2-one (2i): yield 94% (93.8 mg); white solid; mp 123−124 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.86 (d, J = 7.6 Hz, 2 H), 7.48−7.34 (m, 4 H), 7.28 (d, J = 7.6 Hz, 1 H), 7.24−7.17 (m, 2 H), 2.43 (s, 3 H); ^{13}C NMR δ 152.2, 139.6, 136.6, 132.7, 130.1, 129.2, 128.8, 128.7, 128.3, 126.6, 124.9, 124.8, 97.9, 21.3; IR ν (KBr, cm^{-1}) 3057, 1747, 1637, 1611, 1490, 1446, 1379, 1228, 1059, 1026, 976, 738, 692; MS (ESI) m/z 352.1 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}BrNO_2$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.34; H, 3.35; N, 4.05.

4-Bromo-3-(3-methoxyphenyl)-5-phenyl-3H-oxazol-2-one (2j): yield 91% (93.2 mg); white solid; mp 131−132 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.86 (d, J = 7.2 Hz, 2 H), 7.47−7.35 (m, 4 H), 7.04−6.97 (m, 2 H), 6.94 (t, J = 2.0 Hz, 1 H), 3.85 (s, 3 H); ^{13}C NMR δ 160.3, 152.1, 136.7, 133.8, 130.1, 128.8, 128.7, 126.5, 124.9, 119.9, 115.2, 113.5, 97.7, 55.5; IR ν (KBr, cm^{-1}) 3074, 1746, 1598, 1493, 1380, 1255, 1226, 1036, 982, 783, 681; MS (ESI) m/z 368.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}BrNO_3$: C, 55.51; H, 3.49; N, 4.05. Found: C, 55.55; H, 3.52; N, 3.88.

4-Bromo-5-phenyl-3-(o-tolyl)-3H-oxazol-2-one (2k): yield 94% (95.0 mg); white solid; mp 97−98 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.87 (d, J = 7.6 Hz, 2 H), 7.48−7.31 (m, 6 H), 7.26 (d, J = 6.4 Hz, 1 H), 2.29 (s, 3 H); ^{13}C NMR δ 151.7, 137.3, 136.6, 131.7, 131.3, 130.2, 129.2, 128.7, 127.1, 126.6, 124.7, 98.4, 17.6; IR ν (KBr, cm^{-1}) 3071, 1771, 1624, 1491, 1367, 1233, 1057, 1000, 960, 764, 679; MS (ESI) m/z 368.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}BrNO_2$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.01; H, 3.54; N, 4.19.

4-Bromo-3-(2-bromophenyl)-5-phenyl-3H-oxazol-2-one (2l): yield 98% (116.8 mg); white solid; mp 129−130 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.89−7.86 (m, 2

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H), 7.78 (dd, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1 H), 7.53−7.36 (m, 6 H); ^{13}C NMR δ 151.4, 136.8, 133.8, 132.2, 131.7, 131.3, 128.8, 128.7, 128.6, 126.5, 124.8, 124.3, 98.0; IR ν (KBr, cm^{-1}) 3088, 1750, 1711, 1623, 1478, 1379, 1230, 1189, 1051, 966, 762,677; MS (ESI) m/z 416.0 (48) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9Br_2NO_2$: C, 45.61; H, 2.30; N, 3.55. Found: C, 45.76; H, 2.22; N, 3.28.

4-Bromo-5-phenyl-3-(p-tolyl)-3H-oxazol-2-one (**2m**): yield 83% (82.1 mg); white solid; mp 145−146 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.85 (d, J = 7.2 Hz, 2 H), 7.44 (t, J = 7.2 Hz, 2 H), 7.40−7.25 (m, 5 H), 2.42 (s, 3 H); ^{13}C NMR δ 152.3, 139.5, 136.5, 130.2, 130.1, 128.7, 128.6, 127.6, 126.6, 124.9, 98.1, 21.2; IR ν (KBr, cm^{-1}) 3039, 1768, 1619, 1512, 1447, 1371, 1228, 1167, 1058, 1000, 963, 748, 683; MS (ESI) m/z 352.1 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}BrNO_2$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.32; H, 3.32; N, 3.91.

4-Bromo-3-(4-bromophenyl)-5-phenyl-3H-oxazol-2-one (**2n**): yield 64% (80.3 mg); white solid; mp 200−201 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.85 (d, J = 7.2 Hz, 2 H), 7.66 (d, J = 8.8 Hz, 2 H), 7.46 (t, J = 6.4 Hz, 2H), 7.42−7.36 (m, 1 H), 7.31 (d, J = 6.4 Hz, 2 H); ^{13}C NMR δ 151.8, 137.1, 132.7, 131.8, 129.2, 129.0, 128.8, 126.3, 125.0, 123.3, 97.2; IR ν (KBr, cm^{-1}) 3089, 1768, 1485, 1374, 1221, 1061, 1003, 963, 764, 681; MS (ESI) m/z 416.0 (52) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9Br_2NO_2$: C, 45.61; H, 2.30; N, 3.55. Found: C, 45.97; H, 2.33; N, 3.39.

4-Bromo-3-(naphthalen-2-yl)-5-phenyl-3H-oxazol-2-one (**2o**): yield 74% (79.6 mg); white solid; mp 170−171 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 10:1); ^{1}H NMR δ 8.03 (d, J = 8.0 Hz, 1 H), 7.99−7.95 (m, 1 H), 7.94−7.90 (m, 2 H), 7.75−7.70 (m, 1 H), 7.64−7.54 (m, 4 H), 7.48 (t, J = 7.2 Hz, 2 H), 7.43−7.37 (m, 1 H); ^{13}C NMR δ 152.3, 136.8, 134.4, 130.7, 130.5, 129.1, 128.8, 128.7, 128.6, 127.8, 127.7, 127.0, 126.6, 125.3, 124.8, 122.1, 99.2; IR ν (KBr, cm^{-1}) 3062, 1769, 1625, 1404, 1236, 1052, 988, 772, 677; MS (ESI) m/z 388.1 (100) [M + Na]$^+$. Anal. Calcd for $C_{19}H_{12}BrNO_2$: C, 62.32; H, 3.30; N, 3.82. Found: C, 62.71; H, 3.35; N, 3.99.

3-Benzyl-4-bromo-5-phenyl-3H-oxazol-2-one (**2p**): yield 51% (51.5 mg); white solid; mp 122−123 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.77 (d, J = 7.2 Hz, 2 H), 7.45−7.29 (m, 8 H), 4.91 (s, 2 H); ^{13}C NMR δ 153.3, 136.0, 135.3, 128.9, 128.64, 128.59, 128.2, 127.8, 126.6, 124.7, 97.3, 46.7; IR ν (KBr, cm^{-1}) 3058, 1758, 1618, 1362, 1184, 1055, 997, 767, 711; MS (ESI) m/z 352.9 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}BrNO_2$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.32; H, 3.48; N, 4.17.

4-Bromo-3-butyl-5-phenyl-3H-oxazol-2-one (**2q**): yield 53% (46.7 mg); colorless oil; R_f 0.20 (ν_{PE}/ν_{EA} = 40:1); ^{1}H NMR δ 7.78 (d, J = 7.6 Hz, 2 H), 7.42 (t, J = 7.2 Hz, 2 H), 7.33 (t, J = 7.6 Hz, 1 H), 3.71 (t, J = 7.3 Hz, 2 H), 1.79−1.68 (m, 2 H), 1.49−1.38 (m, 2 H), 0.98 (t, J = 7.2 Hz, 3 H); ^{13}C NMR δ 153.0, 135.7, 128.6, 128.4, 126.7, 124.6, 97.4, 43.1, 30.8, 19.7, 13.6; IR ν (KBr, cm^{-1}) 2958, 1767, 1628, 1446, 1358, 1196, 1101, 1051,1027, 984, 749, 695; MS (ESI) m/z 318.1 (100) [M + Na]$^+$; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{14}BrNO_2$ [M + Na]$^+$ 318.0106, found 318.0113.

4-Bromo-5-butyl-3-phenyl-3H-oxazol-2-one (**2r**): yield 54% (47.2 mg); white solid; mp 83−85 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 30:1); ^{1}H NMR δ 7.51−7.45 (m, 2 H), 7.44−7.39 (m, 1 H), 7.38−7.33 (m, 2 H), 2.51 (t, J = 7.2 Hz, 2 H), 1.69−1.60 (m, 2 H), 1.46−1.35 (m, 2 H), 0.96 (t, J = 7.2 Hz, 3 H); ^{13}C NMR δ 153.0, 139.6, 133.2, 129.2, 128.7, 127.2, 97.7, 28.8, 24.7, 21.9, 13.6; IR ν (KBr, cm^{-1}) 2958, 1747, 1665, 1616, 1378, 1222, 1156, 984, 761, 696; MS (ESI) m/z 318.1 (100) [M + Na]$^+$. Anal. Calcd for $C_{13}H_{14}BrNO_2$: C, 52.72; H, 4.76; N, 4.73. Found: C, 52.37; H, 4.89; N, 4.57.

4-Bromo-5-octyl-3-phenyl-3H-oxazol-2-one (**2s**): yield 49% (52.5 mg); white solid; mp 59−60 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 40:1); ^{1}H NMR δ 7.51−7.45 (m, 2 H), 7.44−7.39 (m, 1 H), 7.38−7.33 (m, 2 H), 2.51 (t, J = 7.2 Hz, 2 H), 1.70−1.61 (m, 2 H), 1.41−1.26 (m, 10 H), 0.89 (t, J = 6.8 Hz, 3 H); ^{13}C NMR δ 153.0, 139.7, 133.2, 129.2, 128.7, 127.2, 97.6, 31.8, 29.7, 29.1, 28.8, 26.8, 25.0, 22.6, 14.1; IR ν (KBr, cm^{-1}) 2958, 1747, 1665, 1616, 1378, 1222, 1156, 984, 761, 696; MS (ESI) m/z 374.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{17}H_{22}BrNO_2$: C, 57.96; H, 6.29; N, 3.98. Found: C, 57.88; H, 6.43; N, 3.67.

(E)-4-Bromo-3-(2-bromophenyl)-5-styryl-3H-oxazol-2-one (**2t**): yield 71% (89.8 mg); white solid; mp 149−150 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.76 (d, J = 8.0 Hz, 1 H), 7.52−7.46 (m, 3 H), 7.43−7.35 (m, 4 H), 7.30 (t, J = 7.2 Hz, 1 H), 7.07 (d, J = 16.0 Hz, 1 H), 6.68 (d, J = 16.4 Hz, 1 H); ^{13}C NMR δ 151.2, 137.7, 135.9, 133.8, 132.1, 131.7, 131.0, 130.2, 128.8, 128.6, 128.5, 126.7, 124.0, 110.4, 100.2; IR ν (KBr, cm^{-1}) 2924, 1761, 1481, 1446, 1379, 1162, 1234, 1055, 991, 955, 751; MS (ESI) m/z 441.9 (56) [M + Na]$^+$. Anal. Calcd for $C_{17}H_{11}Br_2NO_2$: C, 48.49; H, 2.63; N, 3.33. Found: C, 48.71; H, 2.48; N, 3.57.

4-Chloro-3,5-diphenyl-3H-oxazol-2-one (**3a**): yield 74% (59.4 mg); white solid; mp 139−140 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.80 (d, J = 7.2 Hz, 2 H), 7.53 (t, J = 7.2 Hz, 2 H), 7.50−7.41 (m, 5 H), 7.37 (t, J = 7.6 Hz, 1 H); ^{13}C NMR δ 151.5, 134.4, 131.9, 129.5, 129.1, 128.8, 128.7, 127.3, 126.2, 124.6, 111.2; IR ν (KBr, cm^{-1}) 3081, 1774, 1637, 1383, 1242, 1063, 1018, 975, 761, 695; MS (ESI) m/z 294.0 (100) [M + Na]$^+$. Anal. Calcd for $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71; N, 5.16. Found: C, 66.01; H, 3.86; N, 4.95.

3-(3-Bromophenyl)-4-chloro-5-phenyl-3H-oxazol-2-one (**3g**): yield 84% (87.8 mg); white solid; mp 132−133 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.79 (d, J = 7.6 Hz, 2 H), 7.63−7.58 (m, 2 H), 7.46 (t, J = 7.2 Hz, 2 H), 7.43−7.35 (m, 3 H); ^{13}C NMR δ 151.1, 134.8, 133.1, 132.3, 130.6, 130.3, 128.9, 128.8, 125.95, 125.90, 124.7, 122.7, 110.7; IR ν (KBr, cm^{-1}) 3063, 1764, 1637, 1577, 1477, 1375, 1228, 1182, 1066, 1023, 995, 733, 676; MS (ESI) m/z 372.0 (75) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9BrClNO_2$: C, 51.39; H, 2.59; N, 4.00. Found: C, 51.40; H, 2.50; N, 3.87.

4-Chloro-3-(3-methoxyphenyl)-5-phenyl-3H-oxazol-2-one (**3j**): yield 88% (78.1 mg); white solid; mp 94−95 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.80 (d, J = 7.6 Hz, 2 H), 7.48−7.40 (m, 3 H), 7.37 (t, J = 7.6 Hz, 1 H), 7.01 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 2 H), 6.96 (t, J = 2.0 Hz, 1 H), 3.85 (s, 3 H); ^{13}C NMR δ 160.3, 151.4, 134.4, 132.8, 130.1, 128.8, 128.6, 126.2, 124.6, 119.5, 115.0, 113.0, 111.2, 55.5; IR ν (KBr, cm^{-1}) 2956, 1763, 1634, 1498, 1473, 1380, 1251, 1218, 1041, 987, 778, 695; MS (ESI) m/z 324.1 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}ClNO_3$: C, 63.69; H, 4.01; N, 4.64. Found: C, 63.50; H, 4.25; N, 4.61.

3-(2-Bromophenyl)-4-chloro-5-phenyl-3H-oxazol-2-one (**3l**): yield 87% (94.2 mg); white solid; mp 108−109 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.81 (d, J = 7.2 Hz, 2 H), 7.77 (dd, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1 H), 7.59−7.34 (m, 6 H); ^{13}C NMR δ 150.7, 134.6, 133.9, 131.7, 131.2, 131.1, 128.8, 128.7, 126.2, 124.5, 124.1, 111.6; IR ν (KBr, cm^{-1}) 3062, 1772, 1645, 1478, 1445, 1373, 1244, 1183, 1054, 1015, 974, 775, 733; MS (ESI) m/z 372.0 (78) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9BrClNO_2$: C, 51.39; H, 2.59; N, 4.00. Found: C, 51.51; H, 2.55; N, 3.88.

3-(4-Bromophenyl)-4-chloro-5-phenyl-3H-oxazol-2-one (**3n**): yield 65% (68.3 mg); white solid; mp 183−184 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.78 (d, J = 7.2 Hz, 2 H), 7.66 (d, J = 6.8 Hz, 2 H), 7.46 (t, J = 7.2 Hz, 2 H), 7.41−7.35 (m, 1 H), 7.32 (d, J = 6.8 Hz, 2 H); ^{13}C NMR δ 151.2, 134.8, 132.7, 130.9, 128.85, 128.83, 128.7, 126.0, 124.6, 123.1, 110.7; IR ν (KBr, cm^{-1}) 3067, 1705, 1515, 1314,1224, 1062, 1008, 948, 745, 687; MS (ESI) m/z 372.0 (76) [M + Na]$^+$. Anal. Calcd for $C_{15}H_9BrClNO_2$: C, 51.39; H, 2.59; N, 4.00. Found: C, 51.09; H, 2.50; N, 3.93.

3-Benzyl-4-chloro-5-phenyl-3H-oxazol-2-one (**3p**): yield 81% (70.6 mg); white solid; mp 126−127 °C (n-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 15:1); ^{1}H NMR δ 7.70 (d, J = 7.2 Hz, 2 H), 7.48−7.29 (m, 8 H), 4.89 (s, 2 H); ^{13}C NMR δ 152.6, 135.1, 133.8, 128.9, 128.7, 128.4, 128.3, 127.8, 126.3, 124.3, 110.9, 45.7; IR ν (KBr, cm^{-1}) 3062, 1757, 1642, 1491, 1439, 1382, 1341, 1184, 1056, 1018, 931, 704, 685; MS (ESI) m/z 308.1 (100) [M + Na]$^+$. Anal. Calcd for $C_{16}H_{12}ClNO_2$: C, 67.26; H, 4.23; N, 4.90. Found: C, 67.41; H, 4.16; N, 4.72.

Large-Scale Reaction of Ynamide 1a. The reaction of **1a** (1.41g, 5.0 mmol), $Pd(PPh_3)_4$ (0.15 mmol), $CuBr_2$ (20 mmol), K_2CO_3 (10 mmol), and DMF (30 mL) was carried out at 40 °C under N_2 atmosphere for 1 h, and the progress of the reaction was monitored by TLC analysis. After cooling to room temperature, the reaction mixture

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was quenched with ethyl acetate (30 mL) and washed with water (30 mL). The aqueous phase was extracted twice with EtOAc (3 × 20 mL), and the combined organic layer was dried over anhydrous Na_2SO_4. Filtration and concentration gave the crude product, which was purified by chromatography on silica gel (PE/EtOAc, 12:1) to afford **2a** (1.31 g, 86% yield) as a white solid.

General Procedure for Suzuki–Miyaura Coupling of 4-Bromo-oxazolones with Arylboronic Acids: Typical Procedure III. $Pd(PPh_3)_4$ (5.0 mol %), 4-bromo-oxazolones **2** (0.3 mmol), boronic acids (0.33 mmol), toluene (1.0 mL), ethanol (0.5 mL), and Na_2CO_3 (0.6 mmol) in H_2O (0.5 mL) were loaded into a 10 mL Schlenk tube. The reaction solution was heated to 75 °C for 10 h under nitrogen while being stirred. After completion of the reaction, the reaction solution was neutralized by 5% aqueous HCl, and then the aqueous phase was separated and further extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4, and then the solution was concentrated to give a crude product, which was purified by silica gel flash chromatography on a silica gel column with petroleum ether (PE) and ethyl acetate (EA) as eluent to afford 3,4,5-multisubstituted oxazolones **4**.

3,4,5-Triphenyl-3H-oxazol-2-one (4aa): yield 85% (80.1 mg); white solid; mp 223–224 °C (*n*-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 10:1); ^1H NMR δ 7.41–7.20 (m, 13 H), 7.16–7.14 (m, 2 H); ^{13}C NMR δ 153.6, 135.1, 133.6, 130.3, 129.5, 129.01, 129.00, 128.5, 128.1, 127.9, 127.6, 127.1, 126.9, 125.0, 123.5; IR ν (KBr, cm^{-1}) 1751, 1675, 1641, 1617, 1498, 1396, 768, 619; MS (ESI) *m/z* 336.1 (100) $[M + Na]^+$. Anal. Calcd for $C_{21}H_{15}NO_2$: C, 80.49; H, 4.82; N, 4.47. Found: C, 80.37; H, 5.13; N, 4.55.

3,5-Diphenyl-4-(4-(trifluoromethyl)phenyl)-3H-oxazol-2-one (4ab). yield 78% (88.1 mg); white solid; mp 156–157 °C (*n*-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 12:1); ^1H NMR δ 7.47 (d, *J* = 8.0 Hz, 2 H), 7.39–7.27 (m, 10 H), 7.15–7.10 (m, 2 H); ^{13}C NMR δ 153.4, 136.1, 133.3, 131.3 (d), 130.8, 130.5, 129.3, 128.7, 128.3, 127.1, 126.9, 125.9 (q), 125.4, 124.9 122.2, 122.0; IR ν (KBr, cm^{-1}) 3059, 1774, 1617,1596, 1497, 1376, 1330, 1165, 1125, 1068, 1023, 998, 769, 699; MS (ESI) *m/z* 404.2 (100) $[M + Na]^+$. Anal. Calcd for $C_{22}H_{14}F_3NO_2$: C, 69.29; H, 3.70; N, 3.67. Found: C, 69.26; H, 4.07; N, 3.62.

4-(3,5-Dimethylphenyl)-3,5-diphenyl-3H-oxazol-2-one (4ac): yield 98% (104.0 mg); white solid; mp 175–176 °C (*n*-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 10:1); ^1H NMR δ 7.39 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 2 H), 7.33–7.22 (m, 6 H), 7.17–7.13 (m, 2 H), 6.98 (s, 1 H), 6.83 (s, 2 H), 2.21 (s, 6 H); ^{13}C NMR δ 153.7, 138.6, 134.9, 133.7, 131.2, 128.9, 128.4, 127.9, 127.8, 126.9, 126.8, 124.9, 123.9, 21.1; IR ν (KBr, cm^{-1}); MS (ESI) *m/z* 364.2 (100) $[M + Na]^+$. Anal. Calcd for $C_{23}H_{19}NO_2$: C, 80.92; H, 5.61; N, 4.10. Found: C, 80.67; H, 5.91; N, 3.96.

4,5-Diphenyl-3-(3-(trifluoromethyl)phenyl)-3H-oxazol-2-one (4na): yield 65% (74.1 mg); white solid; mp 140–141 °C (*n*-hexane/ethyl acetate); R_f 0.20 (ν_{PE}/ν_{EA} = 10:1); ^1H NMR δ 7.50 (d, *J* = 7.6 Hz, 1 H), 7.46–7.33 (m, 8 H), 7.30–7.25 (m, 3 H), 7.25–7.21 (m, 2 H); ^{13}C NMR δ 153.2, 135.6, 134.2, 131.5 (q), 130.2, 130.0, 129.8, 129.6, 129.3, 128.6, 128.4, 127.3, 126.6, 125.1, 124.6, 124.4 (q), 123.6 (q), 122.9, 121.9; IR ν (KBr, cm^{-1}) 3074, 1761, 1609, 1493, 1448, 1380, 1326, 1264, 1159, 1125, 1064, 1022, 913, 769, 694; MS (ESI) *m/z* 404.1 (100) $[M + Na]^+$. Anal. Calcd for $C_{22}H_{14}F_3NO_2$: C, 69.29; H, 3.70; N, 3.67. Found: C, 69.51; H, 3.44; N, 3.90.

Reaction Mechanism Studies. *Conditions 1.* To an oven-dried Schlenk tube purged with nitrogen and containing a magnetic stir bar were added **1a** (0.1 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), K_2CO_3 (0.2 mmol), and dry DMF (1.0 mL). The resulting solution was stirred at 40 °C for 20 min. After being cooled to room temperature, the reaction mixture was quenched with ethyl acetate (15 mL) and washed with water (30 mL). The aqueous phase was extracted twice with EtOAc (3 × 10 mL), and the combined organic layer was dried over anhydrous Na_2SO_4. Filtration, evaporation, and chromatography on silica gel (PE/EtOAc, 15:1) afforded **2a′** (58%) as a white solid.

Conditions 2. To an oven-dried Schlenk tube purged with nitrogen and a magnetic stirrer bar were added **1a** (0.3 mmol), $PdCl_2(PPh_3)_2$ (0.015 mmol), $CuCl_2$ (1.2 mmol), K_2CO_3 (0.6 mmol), and dry DMF (2.0 mL), and the resulting solution was stirred at 40 °C for 20 min, After being cooled to room temperature, the reaction mixture was quenched with ethyl acetate (15 mL) and washed with water (30 mL). The aqueous phase was extracted twice with EtOAc (3 × 10 mL), and the combined organic layer was dried over anhydrous Na_2SO_4. Filtration, evaporation, and chromatography on silica gel (PE/EtOAc, 20:1) afforded **3a** (41%) and **2a′** (18%).

Conditions 3. To an oven-dried Schlenk tube purged with nitrogen and a magnetic stirrer bar were added **1a** (0.3 mmol), $Pd(PPh_3)_4$ (0.015 mmol), CuCl (1.2 mmol), K_2CO_3 (0.2 mmol), and dry DMF (2.0 mL), and the resulting solution was stirred at 40 °C for 20 min and monitored by TLC.

Reaction of 2a′. To an oven-dried Schlenk tube purged with nitrogen and a magnetic stirrer bar were added **2a′** (0.3 mmol), $Pd(PPh_3)_4$ (0.015 mmol), $CuCl_2$ (1.2 mmol), K_2CO_3 (0.2 mmol), and dry DMF (2.0 mL), and the resulting solution was stirred at 40 °C for 20 min and monitored by TLC.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H NMR and ^{13}C NMR spectra for all new compounds and X-ray crystallographic data (CIF) for compounds **2a** and **2m**. 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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