

Copper(II)-Catalyzed Alkoxyhalogenation of Alkynyl Ureas and Amides as a Route to Haloalkylidene-Substituted Heterocycles

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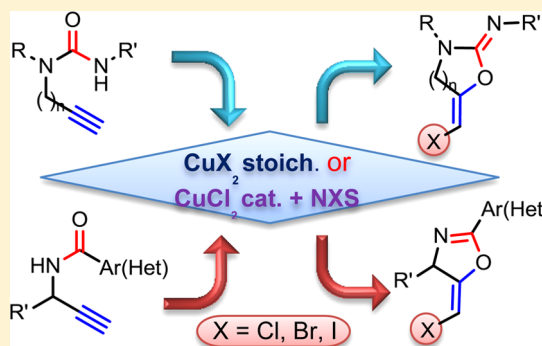
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Supporting Information

ABSTRACT: A highly effective synthesis of haloalkylidene-substituted heterocycles by copper(II)-catalyzed cyclization of alkynyl ureas and secondary amides has been developed. The reaction, which involves a catalytic amount of CuCl₂ and a stoichiometric amount of *N*-halosuccinimide, occurs selectively through an alkoxyhalogenation process. Alternatively, alkoxychlorination and alkoxybromination reactions can be performed working solely with stoichiometric CuCl₂ and CuBr₂, respectively.



INTRODUCTION

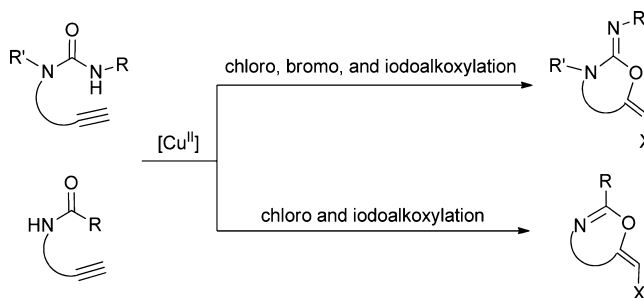
Intramolecular transition-metal-catalyzed alkoxylation of carbon–carbon multiple bonds represents one of the most effective approaches to prepare oxygenated heterocycles, which are important motifs in many biologically active compounds.¹ Processes leading to the generation of new bonds in addition to the first-formed C–O bond have been reported in the literature.² While this approach is substantially devoted to the functionalization of alkenes and allenes, related reactions involving alkynes are somewhat limited.³ Among the procedures of alkoxylation, transition-metal-catalyzed reactions based on the use of secondary amides⁴ or ureas⁵ as nucleophiles represent a useful tool to perform directly functionalized oxygenated heterocycles.

The attractiveness of the copper catalysts stems from their low cost and their tolerance toward many reactive functional groups, and the reactions do not require rigorously anaerobic and anhydrous conditions. These features strongly increased the development of procedures for C–O⁶ and C–N⁷ bond forming reactions. However, despite various kinds of reactivities, the examples of copper-promoted exo-selective intramolecular alkyne hydralkoxylation are rather restricted.⁸ Among these methods, a chlorocyclization of *N*-alkoxy-2-alkynylbenzamides by CuCl₂ and NCS, both in large excess amounts, was reported as a synthetic protocol for isobenzofuran-1-one derivatives.⁹ Recently, the iodocyclization of terminal

propargyl amides in the presence of stoichiometric CuI and Selectfluor was described by Xu and co-workers.¹⁰

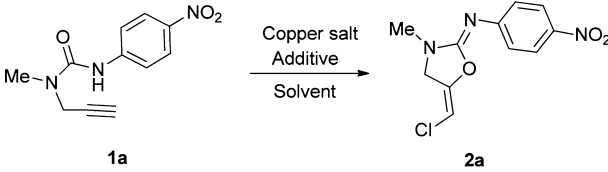
On the basis of the picture emerging from the literature, as part of our ongoing project on intramolecular transition-metal-catalyzed amination and alkoxylation reactions involving C–H and heteroatom–H functionalization,¹¹ we tried to perform a copper-catalyzed alkoxylation/halogenation of alkynyl ureas and secondary amides to afford a range of haloalkylidene-substituted heterocycles (Scheme 1). In principle, the formation of an intramolecular bond with these substrates

Scheme 1. General Copper-Promoted Procedure for Haloalkylidene-Substituted Heterocycles



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Table 1. Optimization of Copper-Promoted Alkoxychlorination Conditions of 4-Nitrophenyl Propargyl Urea 1a



entry	copper salt	additive (equiv)	solvent ^a	time (h)	product (yield (%))
1	CuCl ₂ (1 equiv)		MeCN	2	2a (87)
2	CuCl ₂ (0.5 equiv)		MeCN	2	2a (61)
3	CuCl ₂ (1 equiv)	K ₂ CO ₃ (1)	MeCN	2	2a (84)
4	CuCl ₂ (5 mol %)	NCS (1)	MeCN	5	2a (51)
5	CuCl ₂ (10 mol %)	NCS (1)	MeCN	5	2a (54)
6		NCS (1)	MeCN	8	
7	CuCl ₂ (10 mol %)	LiCl (2)	MeCN	8	2a (3)
8	CuCl (1 equiv)		MeCN	6	
9	CuCl ₂ (5 mol %)	NCS (1)	toluene ^b	3	2a (32)
10	CuCl ₂ (5 mol %)	NCS (1)	THF	3	2a (51)
11	CuCl ₂ (5 mol %)	NCS (1)	DMF ^c	3	
12	CuCl ₂ (5 mol %)	NCS (1)	DCE	6	2a (18)

^aUnless otherwise noted, reactions were carried out at reflux. ^bAt 90 °C. ^cAt 110 °C.

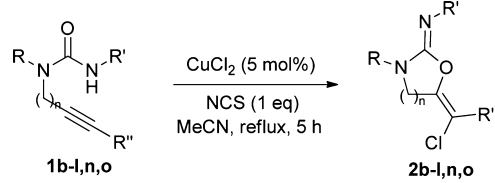
can involve nitrogen and/or oxygen atoms.¹² It is worth noting that the cyclization, when achievable, arises selectively by addition of the oxygen to the triple bond.

RESULTS AND DISCUSSION

The effectiveness of copper(II) salts in the alkoxyhalogenation process was explored on 4-nitrophenyl propargyl urea **1a** (Table 1), which was initially reacted in the presence of CuCl₂ (1 equiv) in acetonitrile at room temperature (entry 1). Interestingly, the oxazole product **2a**, arising from the 5-exo-dig cyclization with the concurrent insertion of a chlorine atom, was isolated in 87% yield. The *E* configuration of the carbon–carbon double bond was assigned by comparison of the NMR spectroscopic data with those reported in the literature for analogous structures.¹³ When the amount of CuCl₂ was split in half (0.5 equiv), the same product was obtained in 61% yield (entry 2). The use of stoichiometric CuCl₂ in the presence of a base such as K₂CO₃ did not improve the yield (entry 3). In attempts to find conditions based on the use of CuCl₂ solely as catalyst, different additives were investigated as possible chlorine sources. NCS was proven to be a fruitful additive (entry 4). When the catalyst loading was increased from 5 to 10 mol %, no substantial improvement in yield was obtained (54% vs 51%) (entry 5). CuCl₂ was essential for the alkoxychlorination process because **1a** failed to react with NCS in its absence (entry 6). The effect of LiCl as a possible alternative source of chlorine was unsatisfactory (entry 7). Stoichiometric CuCl employed as a copper salt without additives furnished unreacted starting material (entry 8). Then, different conditions were evaluated with 5 mol % of CuCl₂ and stoichiometric NCS. Finally, various combinations of solvent and temperature (entries 9–12) did not provide **2a** in higher yield.

To define the scope of the alkoxychlorination reaction, we further explored a range of substituted alkynyl ureas, choosing the catalytic conditions of Table 1, entry 4 (i.e., 5 mol % of CuCl₂ with stoichiometric NCS). First, we investigated the aryl propargyl ureas **1b–i**, which were converted into the (*E*)-5-(chloromethylidene)oxazole derivatives **2b–i** (Table 2, entries 1–9). With the exception of the sole 4-chlorophenyl-substituted oxazole **2d**, the cyclization products were isolated

Table 2. Scope of Cu(II)-Catalyzed Alkoxychlorination of Alkynyl Ureas



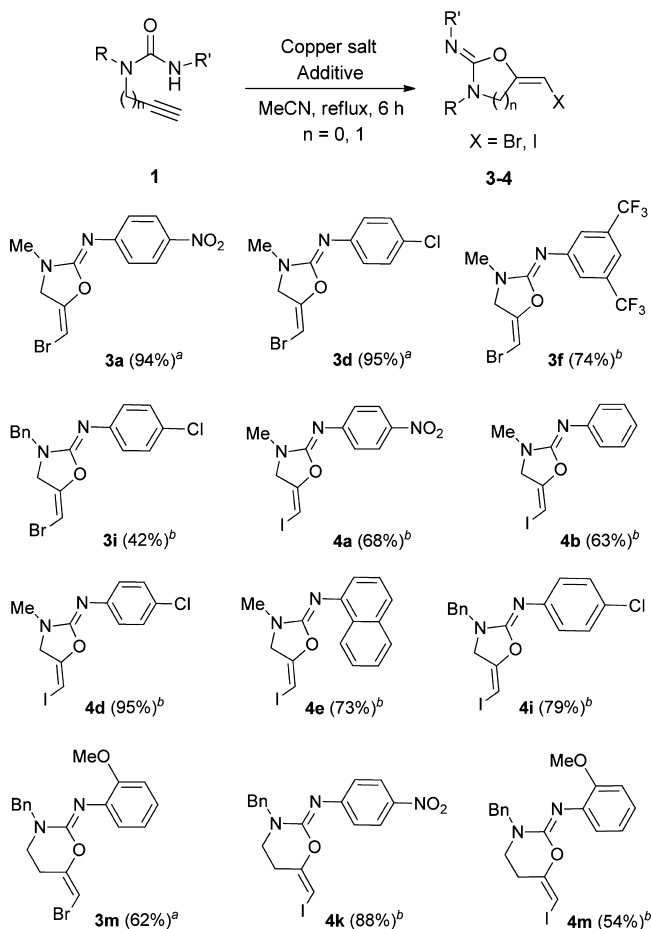
entry	urea	n	R	R'	R''	product (yield (%))
1	1b	1	Me	C ₆ H ₅	H	2b (64)
2	1c	1	Me	4-OMe-C ₆ H ₄	H	2c (82)
3	1d	1	Me	4-Cl-C ₆ H ₄	H	2d (12)
4	1e	1	Me	1-naphthyl	H	2e (98)
5	1f	1	Me	3,5-CF ₃ -C ₆ H ₃	H	2f (75)
6	1g	1	Bn	C ₆ H ₅	H	2g (98)
7	1h	1	Bn	4-NO ₂ -C ₆ H ₄	H	2h (71)
8	1i	1	Bn	4-Cl-C ₆ H ₄	H	2i (85)
9	1j	2	Bn	C ₆ H ₅	H	2j (28)
10	1k	2	Bn	4-NO ₂ -C ₆ H ₄	H	2k (56)
11	1l	2	Bn	1-naphthyl	H	2l (77)
12	1n	1	Me	C ₆ H ₅	C ₆ H ₅	2n (41)
13	1o	1	Me	4-NO ₂ -C ₆ H ₄	4-OMe-C ₆ H ₄	2o (37)

in good to excellent yields. The unsatisfactory outcome of cyclization for urea **1d**, which furnished a complex mixture of tarry products also with use of stoichiometric CuCl₂, was unexpected and could not be ascribed to the presence of the chlorine atom, as evidenced by the behavior of the analogous urea **1i**, which underwent the alkoxychlorination process in 85% yield. These conditions also provided 6-exo-dig-process, as shown by the cyclization of the aryl butynyl ureas **1j–l** that furnished the 1,3-oxazine products, albeit in moderate yields (Table 2, entries 9–11). The cyclization/chlorination reaction was also achieved from the 1,2-disubstituted alkynes **1n,o**, with formation of the corresponding 5-(arylidene)oxazole derivatives (Table 2, entries 12 and 13).

With the successful outcome of the direct alkoxychlorination of alkynyl ureas, we subsequently examined the applicability of

the procedure to prepare bromo- and iodoalkylidene heterocycles. The reaction conditions, conveniently adjusted in term of halogen source, worked well in bromo- and alkoxyiodination processes of propargyl and butynyl ureas (Table 3). More

Table 3. Scope of Alkoxybromination and Alkoxyiodination of Alkynyl Ureas



^aReaction conditions: alkynyl urea (1 mmol), CuBr₂ (1 mmol).

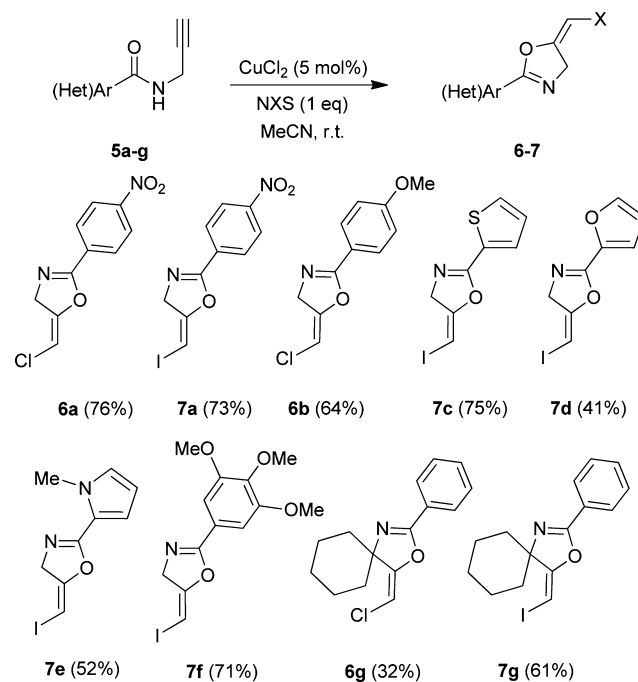
^bReaction conditions: alkynyl urea (1 mmol), CuCl₂ (5 mol %), NXS (1 mmol).

specifically, bromo derivatives 3 were proven to be achievable either with stoichiometric CuBr₂ or with a catalytic amount of CuCl₂ in the presence of a stoichiometric amount of NBS. On the other hand, the treatment of alkynyl ureas with CuCl₂ and stoichiometric NIS provided the formation of the iodomethylidene-substituted oxazole and 1,3-oxazine products 4.¹⁴ The structure and *E* configuration of the alkoxyhalogenation product was unambiguously confirmed by single-crystal X-ray diffraction performed on compound 4i, which revealed the presence of two independent molecules in the asymmetric unit (see the Supporting Information, Figure S1).¹⁵

In view of the importance of vinyl halides as structural motifs, we became interested in exploring other substrates toward alkoxyhalogenation reactions. Using the reaction conditions selected for the alkoxyhalogenation of the alkynyl ureas, the process was performed starting from secondary propargyl (hetero)aryl amides 5. Although alkoxybromination reactions were unfruitful from a synthetic point of view due to the difficult isolation of the product from complex reaction mixtures, the outcome of the reactions was satisfactory to

achieve chloro- and iodooxazole derivatives from aryl amides bearing either electron-withdrawing or electron-donating groups (5a,b,f) (Table 4). Among the propargyl amides of

Table 4. Alkoxyhalogenation Reactions of Secondary (Hetero)aryl Alkynyl Amides^a

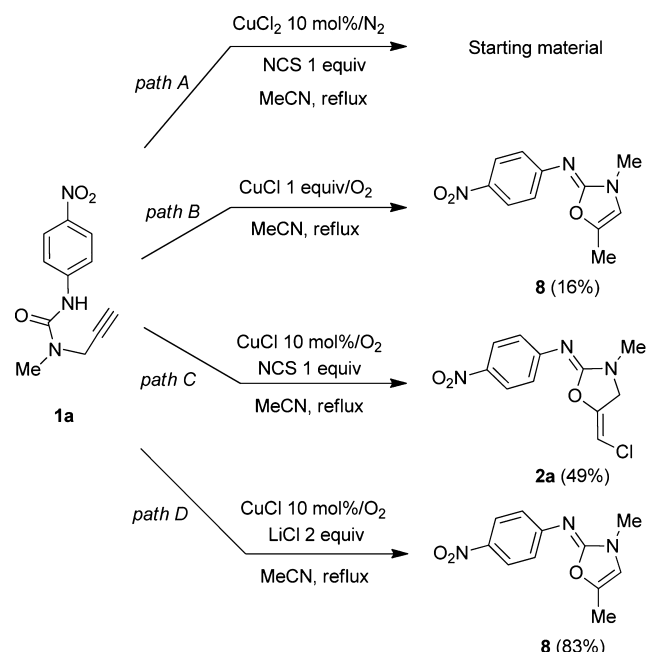


^aReaction conditions: alkynyl amide (1 mmol), CuX₂ (5 mol %), NXS (1 mmol), room temperature, 12–24 h.

monohetero five-membered rings (5c–e), 2-furyl- and 2-(1-methyl)pyrrolyl carboxyamides provided the alkoxyiodination products in lower yields from mixtures enriched in tarry products. Finally, α,α -disubstituted propargyl benzamides (5g) also furnished the expected products, although chloro and iodo substrates were isolated in different yields.

To gain further insights into these reactions, some control experiments were carried out in search of mechanistic evidence. First, we investigated the reaction of the propargyl urea 1a in the presence of catalytic CuCl₂ and stoichiometric NCS in acetonitrile at reflux under a nitrogen atmosphere (Scheme 2, path A). The recovery of the unchanged starting material shows that the presence of molecular oxygen is essential for the outcome of the reaction, probably acting as an oxidant able to renew the Cu(II) catalytic species. To fortify this hypothesis, taking into account the behavior of copper(I) chloride which is unable to promote any reaction, we repeated the experiment of Table 1, entry 8, under a molecular oxygen atmosphere (Scheme 2, path B). The reaction provided only compound 8, albeit isolated in low yield, reasonably arising from the sole intramolecular C–O bond formation, followed by an internal isomerization of the carbon–carbon double bond. The addition of NCS to catalytic CuCl under an oxygen atmosphere gratifyingly provided the chloromethylidene product 2a in 49% yield (Scheme 2, path C). The substitution of NCS with LiCl as an additive led to the hydroalkoxylation/isomerization product 8 instead of the cyclization/chlorination compound 2a, confirming the crucial role of NCS as a source of chlorine (Scheme 2, path D). The different yields shown in paths B and

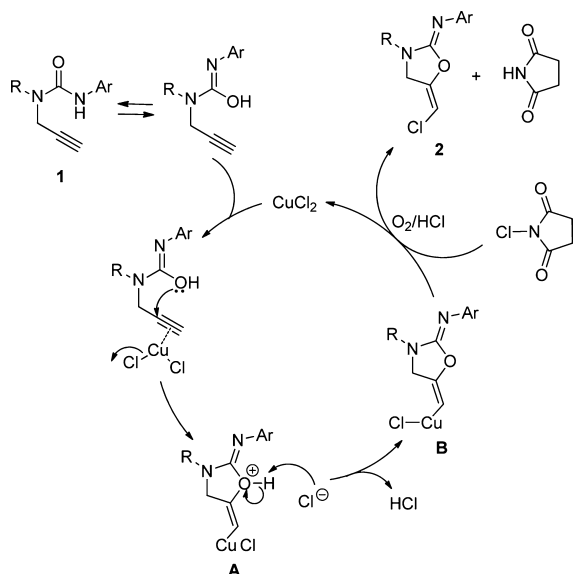
Scheme 2. General Investigations in Search of Further Insights into Copper-Promoted Alkoxyhalogenation Reactions



D could be attributed to a more effective outcome of the cyclization step using a catalytic amount of CuCl.

On the basis of the experimental evidence, a plausible mechanism to explain the alkoxyhalogenation reactions with CuCl₂ and *N*-halosuccinimide is shown in Scheme 3, taking the

Scheme 3. Proposed Mechanism of the Cu(II)-Catalyzed Reaction



alkoxychlorination of the propargyl urea as an example. The catalytic cycle would proceed through the vinyl copper intermediate **A**, generated from an 5-exo-dig cyclization by nucleophilic attack of the oxygen atom on the activated carbon–carbon triple bond.^{7b,i,16} The subsequent deprotonation of **A** forms the intermediate **B**, which is able to interact with NCS, in the presence of HCl and oxygen, providing the

final product **2** and regenerating the copper catalyst. The evolution of intermediate **B** could also proceed by a copper(III) species that undergoes reductive elimination.¹⁷

CONCLUSIONS

In conclusion, we have developed a simple and efficient method of alkoxyhalogenation of alkynyl ureas and secondary amides with copper(II) salts, used in a stoichiometric amount or as a catalyst in the presence of *N*-halosuccinimides. By exploitation of the exocyclic haloalkylidene moiety, the resulting products can undergo further functionalizations, for example by transition-metal-catalyzed reactions, making them versatile building blocks in organic synthesis. These conditions will be tested with alkynyl carbamates and hydroxylamines to improve their general applicability.

EXPERIMENTAL SECTION

General Information. Melting points are uncorrected. IR spectra were recorded on a FT-IR spectrophotometer. Column chromatography was performed on silica gel 60 (mesh size 63–200 μm). Nuclear magnetic resonance spectra were recorded on a 200, 300, or 400 MHz spectrometer for ¹H NMR and a 100 MHz spectrometer for ¹³C NMR. Chemical shifts (δ) for proton nuclear magnetic resonance (¹H NMR) spectra are reported in parts per million downfield relative to the center line of the CDCl₃ triplet at 7.26 ppm. Chemical shifts for carbon nuclear magnetic resonance (¹³C NMR) spectra are reported in parts per million downfield relative to the center line of the CDCl₃ triplet at 77.23 ppm. The abbreviations s, d, t, and m stand for the resonance multiplicities singlet, doublet, triplet, and multiplet, respectively. ¹³C spectra are ¹H decoupled, and multiplicities were determined by the APT pulse sequence.

General Procedure for the Preparation of Ureas 1a–i. To a solution of the alkynyl amine (1 mmol) in THF (5 mL) was added the suitable isocyanate (1 mmol) dropwise. The resulting mixture was stirred at room temperature for 16 h, and then the solvent was removed under reduced pressure; the crude product was pure enough to be used in the subsequent step without further purification.

***N*-Methyl-*N*-(4-nitrophenyl)-*N*'-propargylurea (1a).** Pale yellow solid (230 mg, 99%). Mp: 113 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1655 (C=O). ¹H NMR (400 MHz, CDCl₃): δ 2.35 (t, *J* = 2.4 Hz, 1H), 3.13 (s, 3H), 4.20 (d, *J* = 2.4 Hz, 2H), 7.05 (br s, 1H, missing after deuteration), 7.57 (ddd, *J* = 10.2, 5.1, 3.1 Hz, 2H), 8.14 (ddd, *J* = 10.2, 5.1, 3.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 34.5 (q), 38.2 (t), 73.2 (d), 78.3 (s), 118.7 (d), 125.0 (d), 142.7 (s), 145.1 (s), 154.2 (s). MS (%) ESI: 234 [M + H]⁺. Anal. Calcd for C₁₁H₁₁N₃O₃: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.82; H, 4.98; N, 17.79.

***N*-Methyl-*N*-phenyl-*N*'-propargylurea (1b).** White solid (175 mg, 93%). Mp: 88 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1680 (C=O). ¹H NMR (400 MHz, CDCl₃): δ 2.31 (t, *J* = 2.4 Hz, 1H), 3.07 (s, 3H), 4.17 (d, *J* = 2.4 Hz, 2H), 6.59 (br s, 1H, missing after deuteration), 7.04 (td, *J* = 7.7, 0.6 Hz, 1H), 7.28 (td, *J* = 7.7, 0.6 Hz, 2H), 7.37–7.39 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 34.2 (q), 37.9 (t), 72.6 (d), 78.9 (s), 120.1 (d), 123.3 (d), 128.8 (d), 138.8 (s), 155.3 (s). MS (%) ESI: 189 [M + H]⁺. Anal. Calcd for C₁₁H₁₂N₂O: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.38; H, 6.21; N, 14.65.

***N*-(4-Methoxyphenyl)-*N*'-methyl-*N*'-propargylurea (1c).** Light brown solid (211 mg, 97%). Mp: 77 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1664 (C=O). ¹H NMR (400 MHz, CDCl₃): δ 2.30 (t, *J* = 2.4 Hz, 1H), 3.06 (s, 3H), 3.78 (s, 3H), 4.18 (d, *J* = 2.4 Hz, 2H), 6.41 (br s, 1H, missing after deuteration), 6.83 (d, *J* = 6.9 Hz, 2H), 7.27 (d, *J* = 6.9 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 33.9 (q), 37.8 (t), 55.4 (q), 72.2 (d), 79.3 (s), 113.9 (d), 122.9 (d), 132.1 (s), 155.8 (s), 156.1 (s). MS (%) ESI: 219 [M + H]⁺. Anal. Calcd for C₁₂H₁₄N₂O₂: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.19; H, 6.23; N, 13.10.

***N*-(4-Chlorophenyl)-*N*'-methyl-*N*'-propargylurea (1d).** White solid (217 mg, 98%). Mp: 105–106 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1651 (C=O). ¹H NMR (400 MHz, CDCl₃): δ 2.33 (t, *J* = 2.5 Hz, 1H), 3.08 (s, 3H),

4.18 (d, $J = 2.5$ Hz, 2H), 6.55 (br s, 1H, missing after deuteration), 7.23–7.26 (m, 2H), 7.32–7.34 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 34.3 (q), 38.0 (t), 72.7 (d), 78.7 (s), 121.2 (d), 128.3 (s), 128.8 (d), 137.4 (s), 154.9 (s). MS (%) ESI: 223 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}$: C, 59.33; H, 4.98; N, 12.58. Found: C, 59.05; H, 5.17; N, 12.77.

***N'*-Methyl-*N'*-(1-naphthyl)-*N'*-propargylurea (1e).** White solid (233 mg, 98%). Mp: 111–112 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1648 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.38 (t, $J = 2.4$ Hz, 1H), 3.14 (s, 3H), 4.22 (d, $J = 2.4$ Hz, 2H), 6.89 (br s, 1H, missing after deuteration), 7.43–7.53 (m, 3H), 7.66 (d, $J = 8.2$ Hz, 1H), 7.73 (d, $J = 7.4$ Hz, 1H), 7.85–7.89 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 34.4 (q), 38.2 (t), 72.8 (d), 78.9 (s), 120.9 (d), 121.0 (d), 125.1 (d), 125.7 (d), 125.8 (d), 126.1 (d), 127.9 (s), 128.7 (d), 133.6 (s), 134.1 (s), 156.0 (s). MS (%) ESI: 239 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.46; H, 6.15; N, 11.56.

***N*-[3,5-Bis(trifluoromethyl)phenyl]-*N'*-methyl-*N'*-propargylurea (1f).** Colorless oil (304 mg, 94%). $\nu_{\text{max}}/\text{cm}^{-1}$: 1662 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.37 (t, $J = 2.4$ Hz, 1H), 3.14 (s, 3H), 4.21 (d, $J = 2.4$ Hz, 2H), 6.82 (br s, 1H, missing after deuteration), 7.53 (s, 1H), 7.90 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 34.3 (q), 38.1 (t), 73.2 (d), 78.2 (s), 116.4 (d), 116.6 (d), 119.4 (d), 121.8 (s), 124.5 (s), 131.9 (s), 132.3 (s), 140.3 (s), 154.4 (s). MS (%) ESI: 325 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{13}\text{H}_{10}\text{F}_6\text{N}_2\text{O}$: C, 48.16; H, 3.11; N, 8.64. Found: C, 48.29; H, 2.88; N, 8.85.

***N'*-Benzyl-*N*-phenyl-*N'*-propargylurea (1g).** White solid (92 mg, 35%). Eluent: petroleum ether/AcOEt 3:7. Mp: 68 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1639 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.36 (t, $J = 1.9$ Hz, 1H), 4.20 (d, $J = 1.9$ Hz, 2H), 4.67 (s, 2H), 6.61 (br s, 1H, missing after deuteration), 6.98–7.07 (m, 1H), 7.21–7.46 (m, 9H). ^{13}C NMR (100 MHz, CDCl_3): δ 36.7 (t), 50.7 (t), 73.1 (d), 79.0 (s), 119.9 (d), 123.3 (d), 127.4 (d), 127.9 (d), 128.9 (d), 129.1 (d), 136.8 (s), 138.8 (s), 155.4 (s). MS (%) ESI: 265 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.22; H, 6.24; N, 10.41.

***N'*-Benzyl-*N*-(4-nitrophenyl)-*N'*-propargylurea (1h).** White solid (294 mg, 95%). Mp: 72 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1647 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.41 (t, $J = 2.4$ Hz, 1H), 4.21 (d, $J = 2.4$ Hz, 2H), 4.68 (s, 2H), 7.08 (br s, 1H, missing after deuteration), 7.35–7.47 (m, 7H), 8.11 (d, $J = 7.9$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 36.9 (t), 50.9 (t), 73.7 (d), 78.5 (s), 118.7 (d), 124.9 (d), 127.3 (d), 128.3 (d), 129.2 (d), 136.1 (s), 142.6 (s), 145.1 (s), 154.4 (s). MS (%) ESI: 310 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{O}_3$: C, 66.01; H, 4.89; N, 13.58. Found: C, 65.84; H, 5.19; N, 13.46.

***N'*-Benzyl-*N*-(4-chlorophenyl)-*N'*-propargylurea (1i).** Colorless oil (292 mg, 98%). $\nu_{\text{max}}/\text{cm}^{-1}$: 1663 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.36 (t, $J = 2.5$ Hz, 1H), 4.14 (d, $J = 2.5$ Hz, 2H), 4.63 (s, 2H), 6.88 (br s, 1H, missing after deuteration), 7.20–7.41 (m, 9H). ^{13}C NMR (100 MHz, CDCl_3): δ 36.6 (t), 50.5 (t), 73.2 (d), 78.9 (s), 121.5 (d), 127.4 (d), 128.0 (d), 128.6 (s), 128.7 (d), 129.1 (d), 136.6 (s), 137.5 (s), 155.3 (s). MS (%) ESI: 299 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{ClN}_2\text{O}$: C, 68.34; H, 5.06; N, 9.38. Found: C, 68.46; H, 4.81; N, 9.11.

General Procedure for the Preparation of Ureas 1j–m. To a solution of *N*-benzylbutynylamine¹⁸ (1 mmol) in THF (5 mL) was added the suitable isocyanate (1 mmol) dropwise. The resulting mixture was stirred at room temperature for 16 h, and then the solvent was removed under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: petroleum ether/AcOEt 6/4).

***N'*-Benzyl-*N'*-(butyn-4-yl)-*N*-phenylurea (1j).** Colorless oil (195 mg, 70%). $\nu_{\text{max}}/\text{cm}^{-1}$: 1666 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.10 (t, $J = 2.6$ Hz, 1H), 2.53 (dt, $J = 6.6, 2.6$ Hz, 2H), 3.61 (t, $J = 6.6$ Hz, 2H), 4.67 (s, 2H), 6.69 (br s, 1H, missing after deuteration), 6.99–7.03 (m, 1H), 7.23–7.42 (m, 9H). ^{13}C NMR (100 MHz, CDCl_3): δ 18.6 (t), 47.1 (t), 51.4 (t), 70.6 (d), 82.2 (s), 119.9 (d), 123.0 (d), 127.0 (d), 127.9 (d), 128.9 (d), 129.1 (d), 137.2 (s), 139.1 (s), 155.7 (s). MS (%) ESI: 279 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.83; H, 6.71; N, 9.86.

***N'*-Benzyl-*N'*-(butyn-4-yl)-*N*-(4-nitrophenyl)urea (1k).** Pale yellow oil (252 mg, 78%). $\nu_{\text{max}}/\text{cm}^{-1}$: 1658 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.14 (t, $J = 2.6$ Hz, 1H), 2.54 (dt, $J = 6.4, 2.6$ Hz, 2H), 3.62 (t, $J = 6.4$ Hz, 2H), 4.67 (s, 2H), 7.23 (br s, 1H, missing after deuteration), 7.31–7.44 (m, 7H), 8.10 (d, $J = 9.2$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 18.5 (t), 47.0 (t), 51.4 (t), 71.1 (d), 82.0 (s), 118.4 (d), 124.9 (d), 127.0 (d), 128.1 (d), 129.2 (d), 136.6 (s), 142.4 (s), 145.4 (s), 154.8 (s). MS (%) ESI: 324 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_3$: C, 66.86; H, 5.30; N, 12.90. Found: C, 67.07; H, 5.15; N, 13.14.

***N'*-Benzyl-*N'*-(butyn-4-yl)-*N*-naphthylurea (1l).** Colorless oil (207 mg, 63%). $\nu_{\text{max}}/\text{cm}^{-1}$: 1667 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.09 (t, $J = 2.6$ Hz, 1H), 2.65 (dt, $J = 2.6, 6.4$ Hz, 2H), 3.76–3.80 (m, 2H), 4.79 (s, 2H), 6.80 (br s, 1H, missing after deuteration), 7.11 (d, $J = 8.1$ Hz, 1H), 7.28 (d, $J = 8.0$ Hz, 1H), 7.39–7.49 (m, 7H), 7.60 (d, $J = 8.0$ Hz, 1H), 7.78–7.81 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 18.8 (t), 48.0 (t), 52.2 (t), 70.4 (d), 82.2 (s), 119.9 (d), 120.5 (d), 124.5 (d), 125.6 (d), 125.8 (d), 126.9 (d), 127.3 (s), 128.1 (d), 128.6 (d), 129.3 (d), 133.7 (s), 134.1 (s), 137.2 (s), 156.1 (s). MS (%) ESI: 329 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}$: C, 80.46; H, 6.14; N, 8.53. Found: C, 80.29; H, 6.21; N, 8.75.

***N'*-Benzyl-*N'*-(butyn-4-yl)-*N*-(2-methoxyphenyl)urea (1m).** Colorless oil (206 mg, 67%). $\nu_{\text{max}}/\text{cm}^{-1}$: 1667 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 2.05 (t, $J = 2.6$ Hz, 1H), 2.57 (dt, $J = 2.6, 6.5$ Hz, 2H), 3.66 (s, 3H), 3.67 (t, $J = 6.5$ Hz, 2H), 4.67 (s, 2H), 6.77–6.80 (m, 1H), 6.90–6.95 (m, 2H), 7.17 (br s, 1H, missing after deuteration), 7.26–7.41 (m, 5H), 8.15–8.18 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 18.6 (t), 47.5 (t), 51.9 (t), 55.6 (q), 70.2 (d), 81.8 (s), 109.8 (d), 109.9 (s), 119.0 (d), 119.7 (d), 121.1 (d), 122.0 (d), 122.8 (d), 126.9 (d), 127.7 (d), 128.9 (d), 137.1 (s), 147.7 (s), 155.2 (s). MS (%) ESI: 309 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.17; H, 6.68; N, 8.87.

General Procedure for the Preparation of Ureas 1n,o. To a solution of *N*-methylpropargylurea (1 mmol) in Et_3N (12 mL) under a N_2 atmosphere were added $\text{Pd}(\text{PPh}_3)_4$ (0.05 mmol), CuI (0.1 mmol), and $\text{Ar}'\text{I}$ (1.2 mmol). The resulting mixture was stirred at room temperature for 2 h and then heated to 60 °C for 3 h. The solvent was removed under reduced pressure, and then the crude product was filtered through a short pad of silica with AcOEt and the solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography.

***N'*-Methyl-*N'*-(1-phenylpropyn-3-yl)-*N*-phenylurea (1n).** Colorless oil (108 mg, 41%). Eluent: petroleum ether/AcOEt 6/4. $\nu_{\text{max}}/\text{cm}^{-1}$: 1637 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 3.13 (s, 3H), 4.41 (s, 2H), 6.70 (br s, 1H, missing after deuteration), 7.29–7.46 (m, 10H). ^{13}C NMR (100 MHz, CDCl_3): δ 34.3 (q), 38.8 (t), 84.4 (s), 84.4 (s), 119.1 (d), 120.3 (d), 120.5 (d), 122.2 (s), 122.6 (d), 122.9 (d), 128.4 (d), 128.5 (d), 128.7 (d), 131.8 (d), 132.0 (d), 139.2 (s), 155.6 (s). MS (%) ESI: 265 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.37; H, 5.89; N, 10.69.

***N'*-Methyl-*N'*-[1-(4-methoxyphenyl)propyn-3-yl]-*N*-(4-nitrophenyl)urea (1o).** Pale orange oil (102 mg, 30%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\text{max}}/\text{cm}^{-1}$: 1629 ($\text{C}=\text{O}$). ^1H NMR (400 MHz, CDCl_3): δ 3.17 (s, 3H), 3.82 (s, 3H), 4.40 (s, 2H), 6.85 (d, $J = 8.8$ Hz, 2H), 7.18 (br s, 1H, missing after deuteration), 7.37 (d, $J = 8.8$ Hz, 2H), 7.58 (d, $J = 9.2$ Hz, 2H), 8.15 (d, $J = 9.2$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 30.5 (q), 39.1 (t), 55.3 (q), 81.9 (s), 85.0 (s), 113.3 (d), 114.3 (s), 117.9 (d), 124.9 (d), 133.2 (d), 142.4 (s), 145.6 (s), 154.5 (s), 159.92 (s). MS (%) ESI: 340 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_4$: C, 63.71; H, 5.05; N, 12.38. Found: C, 63.87; H, 4.81; N, 12.21.

**General Procedure for Stoichiometric Intramolecular Alkox-
yhalogenation of Alkynyl Ureas.** A solution of alkynyl urea (1 mmol) and CuX_2 (1 mmol) in MeCN (14 mL) was heated at reflux for 6 h. The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography.

(*E*)-5-(Chloromethylidene)-3-methyl-2-[(4-nitrophenyl)imino]-oxazolidine (2a). Pale yellow oil (232 mg, 87%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\text{max}}/\text{cm}^{-1}$: 1662 ($\text{C}=\text{N}$). ^1H NMR (400 MHz, CDCl_3): δ 3.14 (s, 3H), 4.32 (d, $J = 2.8$ Hz, 2H), 6.00 (t, $J = 2.8$ Hz,

1H), 7.13 (d, $J = 8.7$ Hz, 2H), 8.14 (d, $J = 8.7$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 31.7 (q), 49.8 (t), 96.7 (d), 123.7 (d), 124.6 (d), 142.8 (s), 147.3 (s), 150.6 (s), 152.8 (s). MS (%) ESI: 268 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{11}\text{H}_{10}\text{ClN}_3\text{O}_3$: C, 49.36; H, 3.77; N, 15.70. Found: C, 49.59; H, 3.54; N, 15.85.

(E)-5-(Bromomethylidene)-3-methyl-2-[(4-nitrophenyl)imino]oxazolidine (**3a**). White solid (292 mg, 94%). Eluent: petroleum ether/AcOEt 3/2. Mp: 210–211 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1658 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 3.03 (s, 3H), 4.18 (d, $J = 2.8$ Hz, 2H), 5.90 (t, $J = 2.8$ Hz, 1H), 7.07 (d, $J = 9.0$ Hz, 2H), 8.07 (d, $J = 9.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 31.7 (q), 51.1 (t), 83.3 (d), 123.7 (d), 124.6 (d), 142.7 (s), 148.1 (s), 150.4 (s), 153.2 (s). MS (%) ESI: 312 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{11}\text{H}_{10}\text{BrN}_3\text{O}_3$: C, 42.33; H, 3.23; N, 13.46. Found: C, 42.52; H, 3.47; N, 13.21.

(E)-5-(Bromomethylidene)-2-[(4-chlorophenyl)imino]-3-methyl-oxazolidine (**3d**). Colorless oil (285 mg, 95%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\text{max}}/\text{cm}^{-1}$: 1653 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 3.03 (s, 3H), 4.16 (d, $J = 2.7$ Hz, 2H), 5.86 (t, $J = 2.7$ Hz, 1H), 6.97 (d, $J = 8.7$ Hz, 2H), 7.21 (d, $J = 8.7$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 31.7 (q), 51.1 (t), 82.5 (d), 124.7 (d), 127.6 (s), 128.6 (d), 144.8 (s), 148.5 (s), 149.9 (s). MS: m/z 300 (M^+). Anal. Calcd for $\text{C}_{11}\text{H}_{10}\text{BrClN}_2\text{O}$: C, 43.81; H, 3.34; N, 9.29. Found: C, 43.90; H, 3.58; N, 9.55.

(E)-3-Benzyl-6-(bromomethylidene)-2-[(2-methoxyphenyl)imino]-2,3,4,5-tetrahydro-2H-1,3-oxazine (**3m**). Colorless oil (239 mg, 62%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\text{max}}/\text{cm}^{-1}$: 1641 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 2.74 (t, $J = 5.7$ Hz, 2H), 3.32 (t, $J = 5.7$ Hz, 2H), 3.81 (s, 3H), 4.82 (br s, 2H), 5.77 (s, 1H), 6.82–7.08 (m, 3H), 7.30–7.45 (m, 6H). ^{13}C NMR (CDCl_3): δ 25.1 (t), 41.9 (t), 53.3 (t), 56.0 (q), 89.1 (d), 114.6 (d), 123.5 (d), 127.8 (d), 128.3 (d), 128.9 (d), 131.9 (s), 136.5 (s), 149.4 (s), 152.7 (s), 162.2 (s). MS (%) ESI: 387 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{19}\text{H}_{19}\text{BrN}_2\text{O}_2$: C, 58.93; H, 4.95; N, 7.23. Found: C, 59.19; H, 4.74; N, 7.49.

General Procedure for Catalytic Intramolecular Alkoxyhalogenation of Alkynyl Ureas. A solution of alkynyl urea (1 mmol), CuCl_2 (0.05 mmol), and the suitable NXS (1 mmol) in MeCN (14 mL) was heated at reflux for 6 h. The solvent was removed under reduced pressure, and when required the crude product was purified by silica gel column chromatography.

(E)-5-(Chloromethylidene)-3-methyl-2-(phenylimino)oxazolidine (**2b**). Colorless oil (142 mg, 64%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\text{max}}/\text{cm}^{-1}$: 1643 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 3.01 (s, 3H), 4.17 (d, $J = 2.8$ Hz, 2H), 5.90 (t, $J = 2.8$ Hz, 1H), 7.03–7.09 (m, 3H), 7.29 (t, $J = 7.7$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 31.6 (q), 49.7 (t), 95.7 (d), 122.7 (d), 123.3 (d), 128.6 (d), 146.3 (s), 148.2 (s), 149.5 (s). MS (%) ESI: 223 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}$: C, 59.33; H, 4.98; N, 12.58. Found: C, 59.45; H, 5.29; N, 12.28.

(E)-5-(Chloromethylidene)-2-[(4-methoxyphenyl)imino]-3-methyloxazolidine (**2c**). White solid (207 mg, 82%). Eluent: petroleum ether/AcOEt 6/4. Mp: 137 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1657 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 3.01 (s, 3H), 3.76 (s, 3H), 4.19 (d, $J = 2.8$ Hz, 2H), 5.89 (t, $J = 2.8$ Hz, 1H), 6.82 (d, $J = 8.0$ Hz, 2H), 6.97 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 31.8 (q), 49.8 (t), 55.4 (q), 95.5 (d), 113.9 (d), 124.1 (d), 139.2 (s), 148.1 (s), 149.3 (s), 155.3 (s). MS (%) ESI: 253 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{ClN}_2\text{O}_2$: C, 57.04; H, 5.19; N, 11.09. Found: C, 57.21; H, 4.99; N, 11.37.

(E)-5-(Chloromethylidene)-2-[(4-chlorophenyl)imino]-3-methyl-oxazolidine (**2d**). White solid (30 mg, 12%). Eluent: petroleum ether/AcOEt 7/3. Mp: 188 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1661 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 3.15 (s, 3H), 4.30 (d, $J = 2.8$ Hz, 2H), 5.97 (t, $J = 2.8$ Hz, 1H), 7.04 (d, $J = 8.7$ Hz, 2H), 7.22 (d, $J = 8.7$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 32.1 (q), 50.3 (t), 97.2 (d), 124.8 (d), 128.8 (d), 142.4 (s), 147.4 (s), 151.2 (s), 167.3 (s). MS (%) ESI: 257 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{11}\text{H}_{10}\text{Cl}_2\text{N}_2\text{O}$: C, 51.38; H, 3.92; N, 10.90. Found: C, 51.60; H, 3.73; N, 11.15.

(E)-5-(Chloromethylidene)-3-methyl-2-[(1-naphthyl)imino]oxazolidine (**2e**). Pale yellow oil (266 mg, 98%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\text{max}}/\text{cm}^{-1}$: 1668 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 3.12 (s, 3H), 4.20 (d, $J = 2.7$ Hz, 2H), 5.85 (t, $J = 2.7$ Hz, 1H), 7.18 (d, $J = 7.3$ Hz, 1H), 7.43–7.51 (m, 3H), 7.59 (d, $J = 8.2$ Hz, 1H), 7.84 (dd, $J = 6.4$, 3.3 Hz, 1H), 7.25 (dd, $J = 6.4$, 3.3 Hz, 1H). ^{13}C

NMR (100 MHz, CDCl_3): δ 31.8 (q), 49.9 (t), 95.7 (d), 117.9 (d), 122.7 (d), 124.1 (d), 125.1 (d), 125.9 (d), 127.8 (d), 129.3 (s), 134.3 (s), 142.7 (s), 148.0 (s), 149.6 (s). MS (%) ESI: 273 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{13}\text{H}_{13}\text{ClN}_2\text{O}$: C, 66.06; H, 4.80; N, 10.27. Found: C, 65.87; H, 5.11; N, 10.51.

(E)-2-[3,5-Bis(trifluoromethyl)phenylimino]-5-(chloromethylidene)-3-methyloxazolidine (**2f**). Colorless oil (268 mg, 75%). Eluent: petroleum ether/AcOEt 6/4. $\nu_{\text{max}}/\text{cm}^{-1}$: 1668 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 3.10 (s, 3H), 4.30 (d, $J = 2.8$ Hz, 2H), 5.99 (t, $J = 2.8$ Hz, 1H), 7.50 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 31.9 (q), 50.2 (t), 97.9 (d), 116.6 (d), 123.3 (q, $J = 271.3$ Hz), 123.9 (d), 131.9 (q, $J = 33.2$ Hz), 145.9 (s), 147.0 (s), 151.7 (s). MS (%) ESI: 359 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{13}\text{H}_3\text{ClF}_6\text{N}_2\text{O}$: C, 43.53; H, 2.53; N, 7.81. Found: C, 43.76; H, 2.29; N, 7.99.

(E)-3-Benzyl-5-(chloromethylidene)-2-(phenylimino)oxazolidine (**2g**). Colorless oil (292 mg, 98%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\text{max}}/\text{cm}^{-1}$: 1632 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 4.12 (d, $J = 2.9$ Hz, 2H), 4.74 (br s, 2H), 5.91 (t, $J = 2.9$ Hz, 1H), 7.06–7.11 (m, 3H), 7.27–7.44 (m, 7H). ^{13}C NMR (100 MHz, CDCl_3): δ 47.2 (t), 48.8 (t), 96.3 (d), 119.9 (d), 123.3 (d), 123.7 (d), 128.1 (d), 128.4 (d), 128.9 (d), 145.3 (s), 148.1 (s), 149.9 (s), 171.1 (s). MS (%) ESI: 299 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{ClN}_2\text{O}$: C, 68.34; H, 5.06; N, 9.38. Found: C, 68.58; H, 5.17; N, 9.21.

(E)-3-Benzyl-5-(chloromethylidene)-2-[(4-nitrophenyl)imino]oxazolidine (**2h**). Colorless oil (243 mg, 71%). Eluent: petroleum ether/AcOEt 6/4. $\nu_{\text{max}}/\text{cm}^{-1}$: 1590 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 4.16 (d, $J = 2.9$ Hz, 2H), 4.68 (s, 2H), 5.99 (t, $J = 2.9$ Hz, 1H), 7.17 (d, $J = 9.0$ Hz, 2H), 7.35–7.44 (m, 5H), 8.15 (d, $J = 9.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 47.1 (t), 48.7 (t), 97.0 (d), 123.8 (d), 124.7 (d), 124.9 (d), 125.1 (d), 128.3 (d), 128.6 (d), 135.0 (s), 142.8 (s), 147.5 (s), 150.3 (s), 153.0 (s). MS (%) ESI: 344 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{O}_3$: C, 59.40; H, 4.10; N, 12.22. Found: C, 59.58; H, 3.78; N, 12.31.

(E)-3-Benzyl-5-(chloromethylidene)-2-[(4-chlorophenyl)imino]oxazolidine (**2i**). Colorless oil (282 mg, 85%). Eluent: petroleum ether/AcOEt 6/4. $\nu_{\text{max}}/\text{cm}^{-1}$: 1669 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 4.10 (d, $J = 2.8$ Hz, 2H), 4.63 (s, 2H), 5.92 (t, $J = 2.8$ Hz, 1H), 7.03 (d, $J = 8.8$ Hz, 2H), 7.24 (d, $J = 8.8$ Hz, 2H), 7.37–7.41 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3): δ 47.1 (t), 48.7 (t), 96.1 (d), 124.7 (d), 127.7 (s), 128.8 (d), 128.9 (d), 129.1 (d), 129.2 (d), 135.5 (s), 144.8 (s), 148.0 (s), 149.3 (s). MS (%) ESI: 333 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{17}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}$: C, 61.28; H, 4.23; N, 8.41. Found: C, 61.11; H, 4.40; N, 8.69.

(E)-3-Benzyl-6-(chloromethylidene)-2-(phenylimino)-2,3,4,5-tetrahydro-2H-1,3-oxazine (**2j**). Colorless oil (87 mg, 28%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\text{max}}/\text{cm}^{-1}$: 1641 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 2.79 (td, $J = 6.3$, 1.5 Hz, 2H), 3.28 (t, $J = 6.3$ Hz, 2H), 4.82 (s, 2H), 5.88 (t, $J = 1.5$ Hz, 1H), 7.01–7.05 (m, 3H), 7.26–7.42 (m, 7H). ^{13}C NMR (100 MHz, CDCl_3): δ 23.4 (t), 41.8 (t), 53.3 (t), 101.6 (d), 122.4 (d), 123.6 (d), 127.7 (d), 128.2 (d), 128.4 (d), 128.5 (d), 128.7 (d), 136.7 (s), 140.9 (s), 146.2 (s), 148.9 (s). MS (%) ESI: 313 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{18}\text{H}_{17}\text{ClN}_2\text{O}$: C, 69.12; H, 5.48; N, 8.96. Found: C, 69.31; H, 5.62; N, 8.65.

(E)-3-Benzyl-6-(chloromethylidene)-2-[(4-nitrophenyl)imino]-2,3,4,5-tetrahydro-2H-1,3-oxazine (**2k**). Colorless oil (199 mg, 56%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\text{max}}/\text{cm}^{-1}$: 1641 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 2.84 (t, $J = 6.1$ Hz, 2H), 3.36 (t, $J = 6.1$ Hz, 2H), 4.84 (s, 2H), 5.94 (br s, 1H), 7.11 (d, $J = 8.6$ Hz, 2H), 7.34–7.40 (m, 5H), 8.15 (d, $J = 8.6$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 22.9 (t), 42.0 (t), 53.7 (t), 102.6 (d), 123.9 (d), 124.6 (d), 128.0 (d), 128.1 (d), 128.9 (d), 135.9 (s), 142.5 (s), 145.1 (s), 147.1 (s), 148.3 (s). MS (%) ESI: 358 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{ClN}_3\text{O}_3$: C, 60.42; H, 4.51; N, 11.74. Found: C, 60.71; H, 4.29; N, 11.95.

(E)-3-Benzyl-6-(chloromethylidene)-2-(naphthylimino)-2,3,4,5-tetrahydro-2H-1,3-oxazine (**2l**). Colorless oil (278 mg, 77%). Eluent: petroleum ether/AcOEt 6/4. $\nu_{\text{max}}/\text{cm}^{-1}$: 1641 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 2.81–2.85 (m, 2H), 3.37 (t, $J = 6.2$ Hz, 2H), 4.91 (s, 2H), 5.73 (s, 1H), 6.97 (d, $J = 7.8$ Hz, 1H), 7.33–7.58 (m, 9H), 7.95–8.08 (m, 1H), 8.12–8.24 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 23.3 (t), 42.2 (t), 53.6 (t), 101.6 (d), 113.8 (s), 117.9 (d),

124.2 (d), 124.7 (d), 125.0 (s), 125.4 (d), 126.0 (d), 126.3 (d), 126.7 (d), 127.7 (d), 128.8 (d), 129.4 (s), 131.2 (s), 136.9 (s), 142.7 (s). MS (%) ESI: 363 [M + H]⁺. Anal. Calcd for C₂₂H₁₉ClN₂O: C, 72.82; H, 5.28; N, 7.72. Found: C, 72.98; H, 5.12; N, 8.05.

(Z)-5-[Chloro(phenyl)methylidene]-3-methyl-2-(phenylimino)-oxazolidine (**2n**). Colorless oil (122 mg, 41%). Eluent: petroleum ether/AcOEt 6/4. $\nu_{\max}/\text{cm}^{-1}$: 1668 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 3.13 (s, 3H), 4.41 (s, 2H), 7.24–7.46 (m, 10H). ¹³C NMR (100 MHz, CDCl₃): δ 34.4 (q), 38.9 (t), 83.9 (s), 84.6 (s), 120.3 (d), 122.4 (s), 123.4 (d), 128.4 (d), 128.6 (d), 128.8 (d), 131.8 (d), 137.6 (s), 138.8 (s), 155.5 (s). MS (%) ESI: 299 [M + H]⁺. Anal. Calcd for C₁₇H₁₅ClN₂O: C, 68.34; H, 5.06; N, 9.38. Found: C, 68.19; H, 5.35; N, 9.62.

(Z)-5-[Chloro(4-methoxyphenyl)methylidene]-3-methyl-2-[(4-nitrophenyl)imino]oxazolidine (**2o**). White solid (138 mg, 37%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\max}/\text{cm}^{-1}$: 1671 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 3.19 (s, 3H), 3.84 (s, 3H), 4.51 (s, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 8.13 (d, *J* = 8.5 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 31.8 (q), 52.1 (t), 55.4 (q), 111.2 (s), 113.7 (d), 123.7 (d), 124.6 (d), 128.6 (d), 139.9 (s), 142.8 (s), 145.6 (s), 151.5 (s), 152.5 (s), 159.7 (s). MS (%) ESI: 374 [M + H]⁺. Anal. Calcd for C₁₈H₁₆ClN₃O₄: C, 57.84; H, 4.31; N, 11.24. Found: C, 57.99; H, 4.04; N, 11.47.

(E)-5-(Bromomethylidene)-2-[3,5-bis(trifluoromethyl)-phenylimino]-3-methyloxazolidine (**3f**). Colorless oil (297 mg, 74%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\max}/\text{cm}^{-1}$: 1653 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 3.08 (s, 3H), 4.24 (d, *J* = 2.7 Hz, 2H), 5.96 (t, *J* = 2.7 Hz, 1H), 7.47 (br s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 31.7 (q), 51.2 (t), 83.7 (d), 116.1 (d), 123.7 (d), 123.4 (q, *J* = 270.8 Hz), 131.8 (q, *J* = 32.5 Hz), 147.2 (s), 147.8 (s), 151.2 (s). MS (%) ESI: 403 [M + H]⁺. Anal. Calcd for C₁₃H₉BrF₆N₂O: C, 38.73; H, 2.25; N, 6.95. Found: C, 38.43; H, 2.06; N, 7.13.

(E)-3-Benzyl-5-(bromomethylidene)-2-[(4-chlorophenyl)imino]-oxazolidine (**3i**). Colorless oil (157 mg, 42%). Eluent: petroleum ether/AcOEt 4/1. $\nu_{\max}/\text{cm}^{-1}$: 1641 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 4.06 (d, *J* = 2.8 Hz, 2H), 4.68 (s, 2H), 5.89 (t, *J* = 2.7 Hz, 1H), 7.04 (d, *J* = 8.6 Hz, 2H), 7.20–7.29 (m, 2H), 7.32–7.46 (m, 5H). ¹³C NMR (100 MHz, CDCl₃): δ 29.7 (t), 48.8 (t), 83.7 (d), 124.9 (d), 128.1 (d), 128.3 (d), 128.7 (d), 129.0 (d), 132.1 (s), 134.8 (s), 143.2 (s), 148.1 (s), 150.8 (s). MS: *m/z* 376 (M⁺). Anal. Calcd for C₁₇H₁₄BrClN₂O: C, 54.06; H, 3.74; N, 7.42. Found: C, 54.10; H, 3.97; N, 7.65.

(E)-5-(Iodomethylidene)-3-methyl-2-[(4-nitrophenyl)imino]-oxazolidine (**4a**). White solid (244 mg, 68%). Eluent: petroleum ether/AcOEt 3/2. Mp: 133 °C. $\nu_{\max}/\text{cm}^{-1}$: 1642 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 3.11 (s, 3H), 4.22 (d, *J* = 2.7 Hz, 2H), 5.80 (t, *J* = 2.7 Hz, 1H), 7.13 (d, *J* = 9.1 Hz, 2H), 8.14 (d, *J* = 9.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 31.6 (q), 50.5 (d), 53.4 (t), 123.8 (d), 124.6 (d), 142.5 (s), 149.9 (s), 151.3 (s), 153.1 (s). MS: *m/z* 359 (M⁺). Anal. Calcd for C₁₁H₁₀IN₂O₃: C, 36.79; H, 2.81; N, 11.70. Found: C, 37.02; H, 2.52; N, 11.91.

(E)-5-(Iodomethylidene)-3-methyl-2-(phenylimino)oxazolidine (**4b**). Pale yellow oil (197 mg, 63%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\max}/\text{cm}^{-1}$: 1644 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 3.11 (s, 3H), 4.17 (d, *J* = 2.6 Hz, 2H), 5.80 (t, *J* = 2.7 Hz, 1H), 7.02–7.08 (m, 2H), 7.25–7.30 (m, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 31.9 (q), 49.6 (d), 53.6 (t), 122.9 (d), 123.3 (d), 128.7 (d), 145.3 (s), 150.5 (s), 150.6 (s). MS: *m/z* 314 (M⁺). Anal. Calcd for C₁₁H₁₁IN₂O: C, 42.06; H, 3.53; N, 8.92. Found: C, 42.01; H, 3.77; N, 8.59.

(E)-2-[(4-Chlorophenyl)imino]-5-(iodomethylidene)-3-methyloxazolidine (**4d**). Colorless oil (330 mg, 95%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\max}/\text{cm}^{-1}$: 1649 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 2.97 (s, 3H), 4.08 (d, *J* = 2.6 Hz, 2H), 5.64 (t, *J* = 2.6 Hz, 1H), 6.95 (dd, *J* = 6.7, 1.9 Hz, 1H), 7.18 (dd, *J* = 6.7, 1.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 31.6 (q), 49.5 (d), 53.4 (t), 124.8 (d), 128.5 (d), 137.6 (s), 144.9 (s), 150.5 (s), 178.2 (s). MS (%) ESI: 349 [M + H]⁺. Anal. Calcd for C₁₁H₁₀ClIN₂O: C, 37.90; H, 2.89; N, 8.04. Found: C, 38.12; H, 2.61; N, 8.29.

(E)-5-(Iodomethylidene)-2-[(1-naphthyl)imino]-3-methyloxazolidine (**4e**). Colorless oil (266 mg, 73%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\max}/\text{cm}^{-1}$: 1653 (C=N). ¹H NMR (400 MHz, CDCl₃):

δ 3.08 (s, 3H), 4.05 (d, *J* = 2.6 Hz, 2H), 5.62 (t, *J* = 2.6 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.46–7.55 (m, 3H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.87–7.89 (m, 1H), 8.30–8.33 (m, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 31.7 (q), 49.4 (d), 53.5 (t), 118.0 (d), 122.7 (d), 124.2 (d), 125.1 (d), 125.9 (d), 126.0 (d), 127.8 (d), 129.4 (s), 134.3 (s), 142.7 (s), 150.2 (s), 150.7 (s). MS (%) ESI: 365 [M + H]⁺. Anal. Calcd for C₁₅H₁₃IN₂O: C, 49.47; H, 3.60; N, 7.69. Found: C, 49.22; H, 3.89; N, 7.83.

(E)-3-Benzyl-2-[(chlorophenyl)imino]-5-(iodomethylidene)-oxazolidine (**4i**). Colorless oil (334 mg, 79%). Eluent: petroleum ether/AcOEt 4/1. $\nu_{\max}/\text{cm}^{-1}$: 1641 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 3.99 (d, *J* = 2.7 Hz, 2H), 4.63 (s, 2H), 5.68 (t, *J* = 2.7 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 2H), 7.24–7.27 (m, 2H), 7.34–7.43 (m, 5H). ¹³C NMR (100 MHz, CDCl₃): δ 48.7 (t), 49.6 (d), 50.7 (t), 124.8 (d), 128.1 (d), 128.2 (d), 128.6 (d), 128.9 (d), 127.7 (s), 135.6 (s), 144.8 (s), 149.9 (s), 150.6 (s). MS (%) ESI: 425 [M + H]⁺. Anal. Calcd for C₁₇H₁₄ClIN₂O: C, 48.08; H, 3.32; N, 6.60. Found: C, 47.76; H, 3.57; N, 6.43.

(E)-3-Benzyl-6-(iodomethylidene)-2-[(4-nitrophenyl)imino]-2,3,4,5-tetrahydro-2H-1,3-oxazine (**4k**). Colorless oil (395 mg, 88%). Eluent: petroleum ether/AcOEt 7/3. $\nu_{\max}/\text{cm}^{-1}$: 1641 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 2.83 (t, *J* = 6.3 Hz, 2H), 3.32 (t, *J* = 6.3 Hz, 2H), 4.78 (s, 2H), 5.77 (s, 1H), 7.07 (dd, *J* = 7.0, 1.9 Hz, 2H), 7.33–7.39 (m, 5H), 8.13 (dd, *J* = 7.0, 1.9 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 27.3 (t), 42.3 (t), 53.4 (t), 58.2 (d), 123.9 (d), 124.5 (d), 127.9 (d), 128.1 (d), 128.8 (d), 136.2 (s), 142.1 (s), 146.6 (s), 150.9 (s), 154.0 (s). MS (%) ESI: 450 [M + H]⁺. Anal. Calcd for C₁₈H₁₆IN₃O₃: C, 48.12; H, 3.59; N, 9.35. Found: C, 48.15; H, 3.90; N, 9.19.

(E)-3-Benzyl-5-(iodomethylidene)-2-[(2-methoxyphenyl)imino]-2,3,4,5-tetrahydro-2H-1,3-oxazine (**4m**). Colorless oil (234 mg, 54%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\max}/\text{cm}^{-1}$: 1653 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 2.76 (td, *J* = 6.3, 1.2 Hz, 2H), 3.27 (t, *J* = 6.3 Hz, 2H), 3.82 (s, 3H), 4.89 (br s, 2H), 5.64 (s, 1H), 6.87–6.92 (m, 2H), 7.02 (t, *J* = 7.1 Hz, 2H), 7.30–7.39 (m, 3H), 7.45 (d, *J* = 7.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 27.8 (t), 42.3 (t), 53.7 (t), 55.8 (q), 58.1 (d), 111.3 (d), 120.8 (d), 124.6 (d), 127.8 (d), 128.3 (d), 128.7 (d), 136.4 (s), 145.8 (s), 151.1 (s), 152.0 (s), 154.1 (s). MS (%) ESI: 435 [M + H]⁺. Anal. Calcd for C₁₉H₁₉IN₂O₂: C, 52.55; H, 4.41; N, 6.45. Found: C, 52.81; H, 4.59; N, 6.17.

General Procedure for Catalytic Intramolecular Alkoxy-chlorination of Alkynyl Amides. A solution of alkynyl amide^{4b,c} (1 mmol), CuCl₂ (0.05 mmol), and NCS (1 mmol) in MeCN (14 mL) was stirred at room temperature until all reagent disappeared (12–24 h). The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography.

(E)-5-(Chloromethylidene)-2-(4-nitrophenyl)-4,5-dihydrooxazole (**6a**). Colorless oil (180 mg, 76%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\max}/\text{cm}^{-1}$: 1661 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 4.81 (d, *J* = 3.2 Hz, 2H), 6.13 (t, *J* = 3.2 Hz, 1H), 8.14–8.19 (m, 2H), 8.30–8.34 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 58.2 (d), 95.8 (d), 123.8 (d), 129.2 (d), 131.4 (s), 131.9 (s), 149.9 (s), 162.0 (s). MS (%) ESI: 239 [M + H]⁺. Anal. Calcd for C₁₀H₇ClN₂O₃: C, 50.33; H, 2.96; N, 11.74. Found: C, 50.51; H, 2.65; N, 11.88.

(E)-5-(Chloromethylidene)-2-(4-methoxyphenyl)-4,5-dihydrooxazole (**6b**). Colorless oil (142 mg, 64%). Eluent: petroleum ether/AcOEt 3/2. $\nu_{\max}/\text{cm}^{-1}$: 1664 (C=N). ¹H NMR (400 MHz, CDCl₃): δ 3.87 (s, 3H), 4.74 (br s, 2H), 6.07 (br s, 1H), 6.94 (d, *J* = 8.1 Hz, 2H), 7.94 (d, *J* = 8.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 29.7 (t), 55.4 (q), 94.5 (d), 114.0 (d), 114.2 (d), 117.7 (s), 118.4 (s), 129.9 (d), 162.7 (s), 163.0 (s). MS (%) ESI: 224 [M + H]⁺. Anal. Calcd for C₁₁H₁₀ClNO₂: C, 59.07; H, 4.51; N, 6.26. Found: C, 58.79; H, 4.78; N, 6.01.

(E)-4-(Chloromethylidene)-3-oxa-2-phenyl-1-azaspiro[4.5]dec-1-ene (**6g**). Colorless oil (83 mg, 32%). ¹H NMR (200 MHz, CDCl₃): δ 1.23–2.05 (m, 8H), 2.35–2.50 (m, 2H), 6.07 (s, 1H), 7.38–7.54 (m, 3H), 7.99 (d, *J* = 6.0 Hz, 2H). These data are in good agreement with those reported in the literature.^{4b}

General Procedure for Catalytic Intramolecular Alkoxyiodination of Alkynyl Amides. A solution of alkynyl amide (1 mmol), CuCl₂ (0.05 mmol) and NIS (1 mmol) in MeCN (14 mL) was stirred

at room temperature until all reagent disappeared (12–24 h). The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography.

(*E*)-5-(*I*odomethylidene)-2-(4-nitrophenyl)-4,5-dihydrooxazole (**7a**). White solid (240 mg, 73%). Eluent: petroleum ether/AcOEt 7/3. Mp: 125 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1661 (C=N). ^1H NMR (400 MHz, CDCl_3): δ 4.68 (d, J = 3.2 Hz, 2H), 5.88 (t, J = 3.2 Hz, 1H), 8.16 (d, J = 8.6 Hz, 2H), 8.32 (d, J = 8.6 Hz, 2H). ^{13}C NMR (CDCl_3): δ 48.3 (d), 61.4 (t), 123.8 (d), 129.0 (d), 132.2 (s), 149.9 (s), 157.3 (s), 162.2 (s). MS (%) ESI: 331 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{10}\text{H}_7\text{IN}_2\text{O}_3$: C, 36.39; H, 2.14; N, 8.49. Found: C, 36.61; H, 1.88; N, 8.26.

(*E*)-5-(*I*odomethylidene)-2-(thiophen-2-yl)-4,5-dihydrooxazole (**7c**). Pale yellow solid (218 mg, 75%). ^1H NMR (300 MHz, CDCl_3): δ 4.64 (d, J = 3.1 Hz, 2H), 5.84 (t, J = 3.2 Hz, 1H), 7.16 (dd, J = 5.0, 3.7 Hz, 1H), 7.58 (dd, J = 5.0, 1.2 Hz, 1H), 7.77 (d, J = 3.7 Hz, 1H). These data are in good agreement with those reported in the literature.¹⁰

(*E*)-2-(Furan-2-yl)-5-(*I*odomethylidene)-4,5-dihydrooxazole (**7d**). Gray solid (112 mg, 41%). ^1H NMR (300 MHz, CDCl_3): δ 4.64 (d, J = 3.2 Hz, 2H), 5.83 (t, J = 3.2 Hz, 1H), 6.56 (dd, J = 3.5, 1.8 Hz, 1H), 7.12 (d, J = 3.5 Hz, 1H), 7.63 (d, J = 1.8 Hz, 1H). These data are in good agreement with those reported in the literature.¹⁰

(*E*)-5-(*I*odomethylidene)-2-(methylpyrrol-2-yl)-4,5-dihydrooxazole (**7e**). Pale yellow solid (149 mg, 52%). Eluent: petroleum ether/Et₂O 9/1. Mp: 108–109 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1645 (C=N); ^1H NMR (200 MHz, CDCl_3): δ 3.94 (s, 3H), 4.58 (d, J = 3.1 Hz, 2H), 5.69 (t, J = 3.1 Hz, 1H), 6.15 (dd, J = 3.9, 2.6 Hz, 1H), 6.75–6.90 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 37.1 (q), 46.9 (d), 60.7 (t), 108.7 (d), 116.9 (d), 119.4 (s), 129.7 (d), 156.9 (s), 158.5 (s). MS (%) ESI: 289 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_9\text{H}_9\text{N}_2\text{O}$: C, 37.52; H, 3.15; N, 9.72. Found: C, 37.21; H, 3.41; N, 9.47.

(*E*)-5-(*I*odomethylidene)-2-(3,4,5-trimethoxyphenyl)-4,5-dihydrooxazole (**7f**). White solid (266 mg, 71%). Eluent: petroleum ether/AcOEt 4/1. Mp: 107–108 °C. $\nu_{\text{max}}/\text{cm}^{-1}$: 1671 (C=N). ^1H NMR (200 MHz, CDCl_3): δ 3.89–3.96 (m, 9H), 4.69 (d, J = 2.8 Hz, 2H), 7.16 (d, J = 2.8 Hz, 1H), 7.27–7.32 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 35.0 (t), 56.6 (q), 61.2 (d), 104.1 (d), 122.3 (s), 135.8 (s), 140.9 (s), 147.6 (s), 153.8 (s). MS (%) ESI: 376 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{INO}_4$: C, 41.62; H, 3.76; N, 3.73. Found: C, 41.35; H, 4.03; N, 3.51.

(*E*)-4-(*I*odomethylidene)-2-phenyl-3-oxa-1-azaspiro[4.5]dec-1-ene (**7g**). Colorless oil (215 mg, 61%). ^1H NMR (300 MHz, CDCl_3): δ 1.23–2.07 (m, 8H), 2.49–2.59 (m, 2H), 5.74 (s, 1H), 7.41–7.55 (m, 3H), 8.00 (d, J = 6.0 Hz, 2H). These data are in good agreement with those reported in the literature.¹⁰

General Procedure for Stoichiometric Intramolecular Alkoxylation of Urea (1a) (Path B, Scheme 2). A solution of urea **1a** (1 mmol) and CuCl (1 mmol) in MeCN (14 mL) was stirred at reflux under an oxygen atmosphere for 5 h. The solvent was removed under reduced pressure, and the crude product **8** was purified by silica gel column chromatography.

General Procedure for Catalytic Intramolecular Alkoxylation of Urea (1a) (Path D, Scheme 2). A solution of urea **1a** (1 mmol), CuCl (10 mol %), and LiCl (3 mmol) in MeCN (14 mL) was stirred at reflux under an oxygen atmosphere for 5 h. The solvent was removed under reduced pressure, and the crude product **8** was purified by silica gel column chromatography.

3,5-Dimethyl-2-[(4-nitrophenyl)imino]-4,5-dihydrooxazole (**8**). Yellow oil (path B, 37 mg, 16%; path D, 193 mg, 83%). Eluent: petroleum ether/AcOEt 2/1. $\nu_{\text{max}}/\text{cm}^{-1}$: 1641 (C=N); ^1H NMR (400 MHz, CDCl_3): δ 2.03 (d, J = 1.4 Hz, 3H), 3.29 (s, 3H), 6.11 (d, J = 1.4 Hz, 1H), 7.54 (d, J = 8.7 Hz, 2H), 8.32 (d, J = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 11.4 (q), 30.2 (q), 110.4 (d), 117.6 (s), 124.5 (d), 127.0 (d), 141.1 (s), 146.1 (s), 152.6 (s). MS (%) ESI: 234 $[\text{M} + \text{H}]^+$. Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_3$: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.74; H, 5.06; N, 18.29.

■ ASSOCIATED CONTENT

■ Supporting Information

Text, figures, and a CIF file giving ^1H and ^{13}C NMR spectra of new compounds and crystallographic data for compound **4j**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01227.

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Notes

The authors declare no competing financial interest.

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