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Studies on Electrophilic Cyclization of *N*-(Buta-2,3-dienyl)amides with *N*-Bromosuccinimide and its Applications

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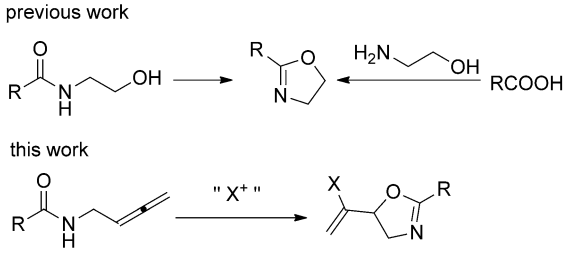
Abstract: An efficient protocol for the synthesis of oxazoline and bisoxazoline derivatives *via* electrophilic cyclization of *N*-(buta-2,3-dienyl)amides with *N*-bromosuccinimide (NBS) at room temperature has been developed. Synthetic transformations of the obtained oxazolines have been successfully performed due to the presence of vinyl bromide units comprising an elimination reaction and a copper(I)-catalyzed C–N coupling reaction using diethylamine (Et_2NH) as the ligand.

Keywords: *N*-(buta-2,3-dienyl)amides; electrophilic cyclization; oxazolines

Introduction

Oxazolines are frequently encountered motifs in natural products and biologically active compounds.[1] They are also known as useful intermediates in organic synthesis and polymer chemistry;[2] furthermore, optically active oxazoline derivatives play an important role in asymmetric synthesis, extensively serving as auxiliaries and ligands.[3] Generally, there are two approaches to oxazolines: (i) the reaction of β-amino alcohols with carboxylic acids and carboxylic acid derivatives;[4] (ii) the cyclodehydration reaction of β-hydroxy amides promoted by Burgess reagent [methyl *N*-(triethylammoniumsulfonyl)carbamate],[5] Vilsmeier reagent (chloromethylene dimethyliminium chloride),[6] DAST,[7] $BF_3{\cdot}Et_2O$[8] and PPh_3/DEAD[9] (Scheme 1). Notably, many of these reagents furnish oxazolines only in moderate yields and are not always in harmony with highly functionalized substrates. Moreover, the diversity of oxazolines is impeded by the limited commercial availability of β-amino alcohols in the above two methods. Due to the importance of the oxazoline nucleus, the development of facile, efficient and diverse synthetic methods is still highly desirable. Electrophilic cyclizations of functionalized allenes have been established as an efficient method for the synthesis of various heterocycles.[10] This methodology profits from the presence of a residual halogen atom which offers potential for the further introduction of various functional groups. On the basis of our continuing interest in this field,[11] we envisioned that the electrophilic cyclization of *N*-(buta-2,3-dienyl)amides[12] may afford an novel approach to α-halovinyloxazolines.

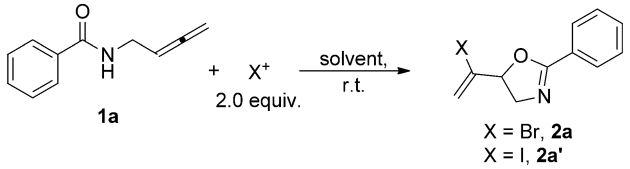


Scheme 1. Known methods for the synthesis of oxazolines and our approach.

Results and Discussion

The initial electrophilic cyclization experiment was conducted by using *N*-(buta-2,3-dienyl)benzamide **1a** and 2.0 equiv. of I_2 in CH_3CN at room temperature. The product of *O*-attack, 5-(1-bromovinyl)-2-phenyl-4,5-dihydrooxazole **2a′**, was detected in 46% yield as determined by ^1H NMR analysis of the crude product (Table 1, entry 1). A series of solvents was examined with no better results (Table 1, entries 2–7). Our pre-

Table 1. Effect of solvent and various electrophilic reagents on the cyclization of *N*-(buta-2,3-dienyl)amide **1a**.[a]



Entry	Solvent	X^+	Time [min]	Yield of **2a**/**2a′** [%][b]
1	CH_3CN	I_2	50	46 (**2a′**)
2	dioxane	I_2	13	36 (**2a′**)
3	THF	I_2	50	38 (**2a′**)
4	CH_2Cl_2	I_2	50	37 (**2a′**)
5[c]	DMF	I_2	40	15 (**2a′**)
6[d]	DMA	I_2	13	33 (**2a′**)
7	toluene	I_2	40	29 (**2a′**)
8	CH_3CN/H_2O (10:1)	I_2	12	46 (**2a′**)
9	CH_3CN/H_2O (4:1)	I_2	15	30 (**2a′**)
10[e]	CH_3CN	I_2	100	29 (**2a′**)
11	CH_3CN	NIS	80	49 (**2a′**)
12	CH_3CN	NBS	15	62 (**2a**)

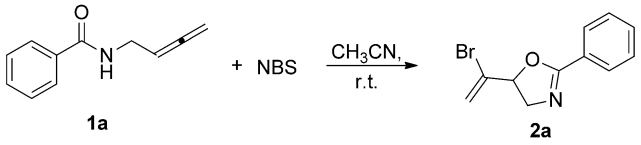
[a] The reaction was carried out with **1a** (0.4 mmol), X^+ (0.8 mmol) in 2 mL of the indicated solvent (dried as described in the Supporting Information) under an argon atmosphere.
[b] Determined by NMR spectroscopic analysis using 1,3,5-trimethylbenzene as the internal standard.
[c] 8% of starting material **1a** remained.
[d] 10% of starting material **1a** remained.
[e] Reaction temperature: 0 °C.

vious work showed that H_2O plays a role in electophilic cyclization.[13] However, a mixture of MeCN and H_2O did not improve the yield here (Table 1, entries 8 and 9). The product was afforded in a relatively poor yield at a lower temperature (0 °C) (Table 1, entry 10). The yields were improved by employing *N*-bromosuccinimide (NBS) instead of *N*-iodosuccinimide (NIS) and I_2 (Table 1, compare entries 1, 11, and 12).

Subsequent study on the effect of the loading of NBS revealed that an increase in the loading of NBS was deleterious for the reaction (Table 2). The results showed that 1.2 equiv. of NBS afforded the best result. Thus, we defined the reaction of *N*-(buta-2,3-dienyl) amides with 1.2 equiv. of NBS in CH_3CN at room temperature as the standard conditions (Table 2, entry 2).

The scope of this transformation was investigated under the standard conditions. As shown in Table 3, the electrophilic cyclization may proceed smoothly for a wide range of substrates with full conversion within 10 min to 5 h. Different electron-withdrawing (NO_2, COOMe, CN, Cl, CF_3, F) (**2b**–**2h**; Table 3, entries 2–8) and electron-donating groups (OMe, Me) (**2i** and **2j**; Table 3, entries 9 and 10) in the phenyl

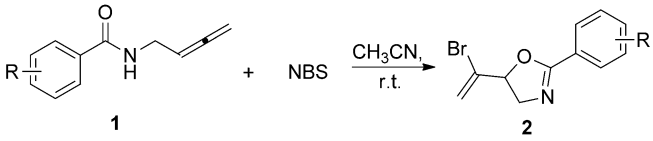
Table 2. Effect of the loading of NBS on the cyclization of *N*-(buta-2,3-dienyl)amide **1a**.[a]



Entry	NBS [equiv.]	Time [min]	Yield of **2a** [%][b]
1	1.0	27	70
2	1.2	10	81
3	2.0	15	62
4	3.0	10	70
5	4.0	21	65
6	5.0	21	56

[a] The reaction was carried out with **1a** (0.4 mmol), NBS (x equiv.) in CH_3CN (2 mL).
[b] Determined by NMR spectroscopic analysis using 1,3,5-trimethylbenzene as the internal standard.

Table 3. Substrate scope for cyclization of *N*-(buta-2,3-dienyl)amides **1** with NBS.[a]

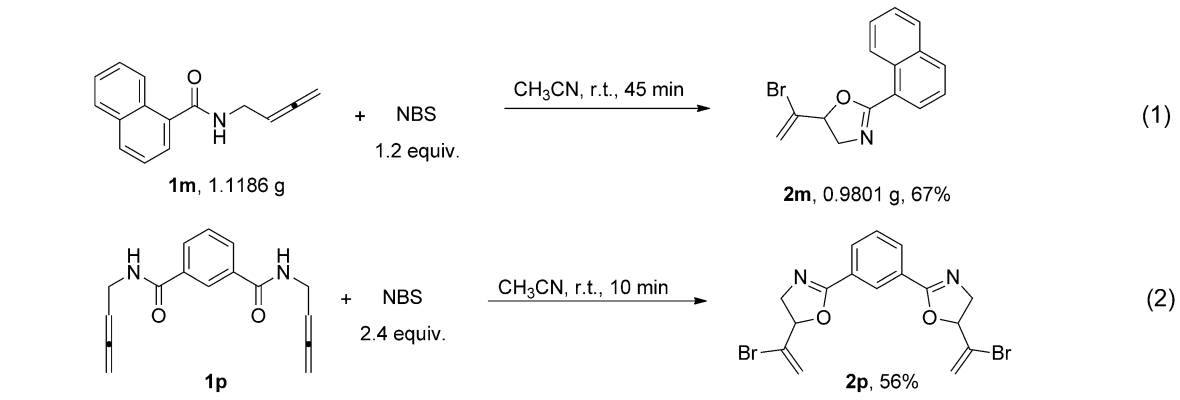


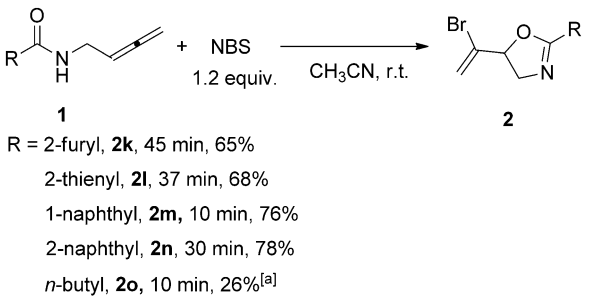
Entry	R	Time [min]	Yield of **2** [%][b]
1	H (**1a**)	10	64 (**2a**)
2	3-NO_2 (**1b**)	80	60 (**2b**)
3	4-CO_2Me (**1c**)	10	74 (**2c**)
4	4-CN (**1d**)	10	81 (**2d**)
5	3,5-Cl_2 (**1e**)	300	77 (**2e**)
6	4-Cl (**1f**)	10	80 (**2f**)
7	4-CF_3 (**1g**)	50	77 (**2g**)
8	4-F (**1h**)	10	78 (**2h**)
9	4-MeO (**1i**)	20	77 (**2i**)
10	3-Me (**1j**)	50	76 (**2j**)

[a] The reaction was carried out with **1** (1.0 mmol) and NBS (1.2 mmol) in CH_3CN (4 mL).
[b] Isolated yield.

ring were tolerated with only limited influence on the yield.

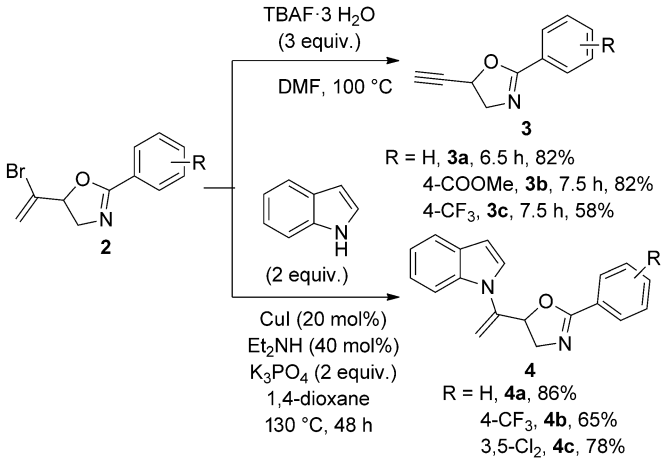
The generality of this transformation was further verified with different types of substrates (Scheme 2): The heteroaromatic substituted oxazolines could be achieved in a preparatively useful yield under the standard conditions (**2k** and **2l**). The presence of naphthyl substituents did not alter the expected outcome of the reaction (**2m** and **2o**). However, when the substrate with an alkyl group was subjected to our standard conditions, the corresponding product (**2o**) was furnished in only 26% isolated yield accompanied by an unidentified side product.





[a] Accompanied by an unknown side product.

Scheme 2. Further substrate scope.



Scheme 3. Synthetic applications of 2-phenyl-5-(1-bromovinyl)-4,5-dihydrooxazoles **2**.

In addition, the reaction may be easily conducted with substrate **1m** on a scale of 1 g affording **2m** in 67% yield [Eq. (1)]. The reaction may also be extended to the synthesis of the bisoxazoline **2p** in 56% yield *via* double bromocyclization of N^1,N^3-di(buta-2,3-dienyl)isophthalamide **1p** [Eq. (2)].

The obtained 2,5-substituted oxazolines could be conveniently converted into synthetically useful building blocks due to the presence of C=C–Br subunits (Scheme 3). The elimination of HBr from **2** afforded the corresponding ethynyloxazolines **3a**–**3c** by treatment with TBAF·3 H_2O.[14] The C–N coupling of **2** with indole, another important heterocycle, was successfully realized using 20 mol% of CuI as catalyst resulting in the formation of **4a** in 86% isolated yield. Interestingly, here the simplest diethylamine (40 mol%) was found to be the most suitable ligand rather than 1,2-diamines which were commonly used as ligands in copper-catalyzed C–N cross-couplings of vinyl halides and amines or azoles.[15] The presence of CF_3 and Cl at the phenyl ring was also tolerated (**4b** and **4c**).

Conclusions

In conclusion, we have developed a facile and efficient protocol for the construction of oxazoline derivatives by electrophilic cyclization of *N*-(buta-2,3-dienyl)amides with the low-cost and readily available reagent NBS. The reaction enjoys features of mild reaction conditions, short reaction time and high tolerance toward functional groups. The bisoxazoline could also been synthesized through this approach. In addition, derivations of the obtained oxazoline derivatives to ethynyloxazolines and 1-(1*H*-indol-1-yl)vinyloxazolines have been achieved. Further studies in this area are being conducted in our laboratory.

Experimental Section

General Information

All reactions were carried out in oven-dried Schlenk tubes. CH_3CN, CH_2Cl_2, DMA and DMF were dried over calcium hydride before distillation. 1,4-Dioxane, THF and toluene

were dried over Na wire before distillation. All the temperatures are referred to the bath temperature. ^{1}H NMR chemical shifts were recorded in ppm in relative to TMS (0.00 ppm). ^{13}C NMR chemical shifts were recorded in ppm in relative to $CDCl_3$ (77.0 ppm). ^{19}F NMR chemical shifts were recorded in ppm relative to $CFCl_3$ (0.00 ppm) (F19CPD). IR spectra were recorded on the infrared spectrometer. Melting points were measured without correction. Common reagents were purchased from commercial sources and were used without further purification. Column chromatography was performed using silica gel (300–400 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. All *N*-(buta-2,3-dienyl)amides **1** were prepared in accordance with the literature procedure.[12]

Synthesis of 5-(1-Bromovinyl)-2-phenyl-4,5-dihydrooxazole (2a); Typical Procedure I

To a dry Schlenk tube were added **1a** (174.0 mg, 1.0 mmol), NBS (213.8 mg, 1.2 mmol), and CH_3CN (4 mL) under an argon atmosphere. The mixture was stirred at room temperature and monitored by TLC. After the reaction was complete, the mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (2 mL) and $Na_2S_2O_3$ (2 mL). The resulting mixture was extracted with ether (10 mL× 3) and dried over anhydrous $MgSO_4$. After filtration and evaporation, chromatography on silica gel (petroleum ether/ethyl acetate = 20:1 to 10:1) afforded **2a** as a solid; yield: 162.9 mg (64%); mp 55–56 °C (*n*-hexane/diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01–7.94 (m, 2H, ArH), 7.54–7.39 (m, 3H, ArH), 6.00 (dd, J = 2.1, 1.2 Hz, 1H, one proton in C=CH_2), 5.62 (d, J = 2.4 Hz, 1H, one proton in C=CH_2), 5.18 (dd, J = 10.0, 7.0 Hz, 1H, OCH), 4.25 (dd, J = 15.0, 9.9 Hz, 1H, one proton in NCH_2), 4.03 (dd, J = 15.0, 7.0 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.4, 131.52, 131.50, 128.4, 128.1, 127.1, 117.7, 81.3, 60.5; IR (neat): ν = 1652, 1448, 1344, 1300, 1275, 1252, 1059, 1008 cm^{-1}; MS (EI): m/z = 253 [M(^{81}Br)$^+$, 5.45], 251 [M(^{79}Br)$^+$, 5.66], 117 (100); anal. calcd. for $C_{11}H_{10}BrNO$: C 52.41, H 4.00, N 5.56; found: C 52.42, H 3.98, N 5.33.

The following compounds were prepared according to Typical Procedure I.

5-(1-Iodovinyl)-2-phenyl-4,5-dihydrooxazole (2a′): To a dry Schlenk tube were added **1a** (1.1125 g, 6.4 mmol), NIS (1.6170 g, 7.2 mmol), and CH_3CN (10 mL) under an argon atmosphere. The mixture was stirred at room temperature for 5 h as monitored by TLC, it was then quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) and $Na_2S_2O_3$ (5 mL). The resulting mixture was extracted with ether (50 mL) and dried over anhydrous $MgSO_4$. After filtration and evaporation, chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) afforded **2a′** as an oil; yield: 0.7358 g (38%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.93 (m, 2H, ArH), 7.52–7.37 (m, 3H, ArH), 6.45 (dd, J = 1.8, 1.2 Hz, 1H, one proton in C=CH_2), 5.89 (d, J = 1.5 Hz, 1H, one proton in C=CH_2), 4.91 (dd, J = 9.9, 7.2 Hz, 1H, OCH), 4.20 (dd, J = 15.3, 9.9 Hz, 1H, one proton in NCH_2), 3.88 (dd, J = 15.3, 7.2 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2, 131.4, 128.3, 128.1, 127.1, 126.0, 110.5, 83.5, 61.4; IR (neat): ν = 1650, 1350, 1254, 1060, 1023 cm^{-1}; MS (EI): m/z = 299 (M$^+$, 13.57), 117 (100); HR-MS: m/z = 298.9809, calcd. for $C_{11}H_{10}INO$ [M$^+$]: 298.9807.

5-(1-Bromovinyl)-2-(3-nitrophenyl)-4,5-dihydrooxazole (2b): The reaction of **1b** (218.0 mg, 1.0 mmol), NBS (213.2 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2b** as a solid (petroleum ether/ethyl acetate = 10:1); yield: 179.8 mg (60%); mp 65–65.3 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.80 (t, J = 1.8 Hz, 1H, ArH), 8.39–8.28 (m, 2H, ArH), 7.64 (t, J = 8.1 Hz, 1H, ArH), 6.04 (dd, J = 2.2, 0.8 Hz, 1H, one proton in C=CH_2), 5.68 (d, J = 2.1 Hz, 1H, one proton in C=CH_2), 5.26 (dd, J = 9.9, 7.2 Hz, 1H, OCH), 4.31 (dd, J = 15.4, 10.4 Hz, 1H, one proton in NCH_2), 4.08 (dd, J = 15.3, 7.2 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 148.0, 133.8, 130.9, 129.5, 128.8, 125.9, 123.1, 118.6, 81.9, 60.5; IR (neat) 1652, 1625, 1524, 1445, 1345, 1299, 1251, 1171, 1107, 1074 cm^{-1}; MS (EI): m/z = 298 [M(^{81}Br)$^+$, 4.13], 296 [M (^{79}Br)$^+$, 4.05], 162 (100); anal. calcd. for $C_{11}H_9BrN_2O_3$: C 44.47, H 3.05, N 9.43; found: C 44.56, H 3.15, N 9.07.

5-(1-Bromovinyl)-2-(4-methoxycarbonylphenyl)-4,5-dihydrooxazole (2c): The reaction of **1c** (231.4 mg, 1.0 mmol), NBS (212.9 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2c** as a solid (petroleum ether/ethyl acetate = 30:1 to 10:1); yield: 232.9 mg (74%); mp 109–110 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13–8.00 (m, 4H, ArH), 6.02 (dd, J = 2.1, 0.6 Hz, 1H, one proton in C=CH_2), 5.65 (d, J = 2.1 Hz, 1H, one proton in C=CH_2), 5.22 (dd, J = 9.9, 7.2 Hz, 1H, OCH), 4.28 (dd, J = 15.3, 10.2 Hz, 1H, one proton in NCH_2), 4.06 (dd, J = 15.3, 7.2 Hz, 1H, one proton in NCH_2), 3.95 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 162.6, 132.6, 131.2, 131.1, 129.6, 128.1, 118.1, 81.5, 60.5, 52.3; IR (neat): ν = 1713, 1648, 1435, 1409, 1347, 1278, 1255, 1193, 1106, 1066, 1009 cm^{-1}; MS (EI): m/z = 311 [M(^{81}Br)$^+$, 4.78], 309 [M(^{79}Br)$^+$, 5.27], 175 (100); anal. calcd. for $C_{13}H_{12}BrNO_3$: C 50.34, H 3.90, N 4.52; found: C 50.56, H 3.92, N 4.86.

5-(1-Bromovinyl)-2-(4-cyanophenyl)-4,5-dihydrooxazole (2d): The reaction of **1d** (198.4 mg, 1.0 mmol), NBS (212.9 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2d** as a solid (petroleum ether/ethyl acetate = 30:1 to 10:1); yield: 224.6 mg (81%); mp 109–110 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, J = 8.4 Hz, 2H, ArH), 7.73 (d, J = 8.7 Hz, 2H, ArH), 6.02 (dd, J = 2.4, 0.9 Hz, 1H, one proton in C=CH_2), 5.66 (d, J = 2.1 Hz, 1H, one proton in C=CH_2), 5.24 (dd, J = 10.2, 7.2 Hz, 1H, OCH), 4.29 (dd, J = 15.5, 10.0 Hz, 1H, one proton in NCH_2), 4.07 (dd, J = 15.6, 7.2 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.7, 132.1, 131.1, 131.0, 128.6, 118.5, 118.1, 114.8, 81.7, 60.5; IR (neat): ν = 2226, 1654, 1634, 1321, 1252, 1066 cm^{-1}; MS (EI): m/z = 278 [M(^{81}Br)$^+$, 4.72], 276 [M(^{79}Br)$^+$, 4.59], 142 (100); anal. calcd. for $C_{12}H_9BrN_2O$: C 52.01, H 3.27, N 10.11; found: C 51.99, H 3.44, N 10.07.

5-(1-Bromovinyl)-2-(3,5-dichlorophenyl)-4,5-dihydrooxazole (2e): The reaction of **1e** (243.0 mg, 1.0 mmol), NBS (215.5 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2e** as a solid (petroleum ether/ethyl acetate = 30:1 to 10:1); yield: 247.2 mg (77%); mp 68–69 °C (*n*-hexane/diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, J = 2.1 Hz, 2H, ArH), 7.48 (t, J = 1.8 Hz, 1H, ArH), 6.00 (dd, J = 2.3, 0.8 Hz, 1H, one proton in C=CH_2), 5.65 (d, J = 2.1 Hz, 1H, one proton in C=CH_2), 5.20 (dd, J = 9.8, 7.4 Hz, 1H, OCH), 4.26

(dd, $J=15.3$, 9.9 Hz, 1H, one proton in NCH_2), 4.03 (dd, $J=15.5$, 7.1 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=161.2$, 135.2, 131.4, 131.0, 129.9, 126.6, 118.5, 81.8, 60.5; IR (neat): $\nu=3047$, 1655, 1564, 1336, 1297, 1249, 1086 cm^{-1}; MS (EI): $m/z=325$ [M(^{81}Br, ^{37}Cl, ^{37}Cl)$^+$, 0.85], 323 [M(^{81}Br, ^{37}Cl, ^{35}Cl or ^{79}Br, ^{37}Cl, ^{37}Cl)$^+$, 4.72], 321 [M(^{81}Br, ^{35}Cl, ^{35}Cl or ^{79}Br,^{37}Cl,^{35}Cl)$^+$, 10.09], 319 [M(^{79}Br,^{35}Cl,^{35}Cl)$^+$, 7.33], 185 (100); anal. calcd. for $C_{11}H_8BrCl_2NO$: C 41.16, H 2.51, N 4.36; found: C 41.11, H 2.47, N 4.15.

5-(1-Bromovinyl)-2-(4-chlorophenyl)-4,5-dihydrooxazole (2f): The reaction of **1f** (207.1 mg, 1.0 mmol), NBS (213.9 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2f** as a solid (petroleum ether/ethyl acetate = 20:1 to 10:1); yield: 231.5 mg (80%); mp 62–63 °C (*n*-hexane/diethyl ether); ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.94$–7.86 (m, 2H, ArH), 7.44–7.37 (m, 2H, ArH), 5.99 (dd, $J=2.1$, 0.9 Hz, 1H, one proton in C=CH_2), 5.63 (d, $J=2.1$ Hz, 1H, one proton in C=CH_2), 5.19 (dd, $J=9.9$, 7.2 Hz, 1H, OCH), 4.24 (dd, $J=15.2$, 10.1 Hz, 1H, one proton in NCH_2), 4.02 (dd, $J=15.5$, 7.1 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=162.2$, 137.5, 131.2, 129.3, 128.5, 125.5, 117.8, 81.3, 60.3; IR (neat): $\nu=1647$, 1596, 1486, 1402, 1349, 1303, 1257, 1168, 1092, 1068, 1008 cm^{-1}; MS (EI): $m/z=289$ [M(^{81}Br,^{37}Cl)$^+$, 2.09], 287 [M(^{81}Br,^{35}Cl or ^{79}Br,^{37}Cl)$^+$, 8.70], 285 [M(^{79}Br,^{35}Cl)$^+$, 6.73], 151 (100); anal. calcd. for $C_{11}H_9BrClNO$: C 46.11, H 3.17, N 4.89; found: C 46.25, H 3.24, N 4.78.

5-(1-Bromovinyl)-2-[4-(trifluoromethyl)phenyl]-4,5-dihydrooxazole (2g): The reaction of **1g** (241.5 mg, 1.0 mmol), NBS (213.7 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2g** as an oil (petroleum ether/ethyl acetate = 10:1); yield: 241.9 mg (77%); ^1H NMR (300 MHz, $CDCl_3$): $\delta=8.09$ (d, $J=8.1$ Hz, 2H, ArH), 7.69 (d, $J=8.4$ Hz, 2H, ArH), 6.01 (dd, $J=2.1$, 0.9 Hz, 1H, one proton in C=CH_2), 5.65 (d, $J=2.1$ Hz, 1H, one proton in C=CH_2), 5.23 (dd, $J=10.2$, 6.9 Hz, 1H, OCH), 4.28 (dd, $J=15.5$, 10.1 Hz, 1H, one proton in NCH_2), 4.06 (dd, $J=15.5$, 7.1 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=162.1$, 133.0 (q, $J=32.4$ Hz), 131.2, 130.5, 128.5, 125.3 (q, $J=3.9$ Hz), 123.6 (q, $J=270.8$ Hz), 118.1, 81.6, 60.5; ^{19}F NMR ($CDCl_3$, 282 MHz): $\delta=-63.5$; IR (neat): $\nu=1655$, 1620, 1412, 1320, 1257, 1166, 1121, 1108, 1701, 1015 cm^{-1}; MS (EI): $m/z=321$ [M(^{81}Br)$^+$, 4.25], 319 [M(^{79}Br)$^+$, 4.41], 185 (100); HR-MS: $m/z=318.9818$, calcd. for $C_{12}H_9{}^{79}BrF_3NO$ [M$^+$]: 318.9820.

5-(1-Bromovinyl)-2-(4-fluorophenyl)-4,5-dihydrooxazole (2h): The reaction of **1h** (191.5 mg, 1.0 mmol), NBS (213.7 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2h** as an oil (petroleum ether/ethyl acetate = 30:1 to 20:1); yield: 212.9 mg (78%); ^1H NMR (300 MHz, $CDCl_3$): $\delta=8.01$–7.95 (m, 2H, ArH), 7.15–7.07 (m, 2H, ArH), 6.00 (dd, $J=2.1$, 1.2 Hz, 1H, one proton in C=CH_2), 5.63 (d, $J=2.1$ Hz, 1H, one proton in C=CH_2), 5.19 (dd, $J=10.1$, 7.1 Hz, 1H, OCH), 4.24 (dd, $J=15.0$, 9.9 Hz, 1H, one proton in NCH_2), 4.02 (dd, $J=15.0$, 6.9 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=164.7$ (d, $J=250.6$ Hz), 162.4, 131.4, 130.4 (d, $J=8.8$ Hz), 123.3 (d, $J=3.0$ Hz), 117.8, 115.5 (d, $J=21.8$ Hz), 81.4, 60.4; ^{19}F NMR ($CDCl_3$, 282 MHz): $\delta=-108.2$; IR (neat): $\nu=1659$, 1605, 1509, 1350, 1206, 1159, 1071 cm^{-1}; MS (EI): $m/z=271$ [M(^{81}Br)$^+$, 6.17], 269 [M(^{79}Br)$^+$, 6.52], 135 (100); HR-MS: $m/z=268.9854$, calcd. for $C_{11}H_9{}^{79}BrFNO$ [M$^+$]: 268.9852.

5-(1-Bromovinyl)-2-(4-methoxy-phenyl)-4,5-dihydrooxazole (2i): The reaction of **1i** (202.8 mg, 1.0 mmol), NBS (213.8 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2i** as a solid (petroleum ether/ethyl acetate = 30:1 to 10:1); yield: 215.6 mg (77%); mp 83–84 °C (*n*-hexane/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.95$–7.88 (m, 2H, ArH), 6.97–6.90 (m, 2H, ArH), 5.99 (dd, $J=2.1$, 0.9 Hz, 1H, one proton in C=CH_2), 5.61 (d, $J=2.1$ Hz, 1H, one proton in C=CH_2), 5.16 (dd, $J=9.9$, 6.9 Hz, 1H, OCH), 4.23 (dd, $J=14.8$, 10.1 Hz, 1H, one proton in NCH_2), 4.00 (dd, $J=14.8$, 6.8 Hz, 1H, one proton in NCH_2), 3.85 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=163.0$, 162.1, 131.6, 129.8, 119.5, 117.4, 113.6, 81.0, 60.3, 55.2; IR (neat): $\nu=1648$, 1606, 1511, 1421, 1347, 1300, 1252, 1164, 1067, 1024 cm^{-1}; MS (EI): $m/z=283$ [M(^{81}Br)$^+$, 13.92], 281 [M(^{79}Br)$^+$, 13.93], 147 (100); anal. calcd. for $C_{12}H_{12}BrNO_2$: C 51.09, H 4.29, N 4.96; found: C 50.96, H 4.49, N 4.88.

5-(1-Bromovinyl)-2-(*m*-tolyl)-4,5-dihydrooxazole (2j): The reaction of **1j** (186.6 mg, 1.0 mmol), NBS (214.0 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2j** as a solid (petroleum ether/ethyl acetate = 10:1); yield: 202.2 mg (76%); mp 67–68 °C (*n*-hexane/diethyl ether); ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.83$–7.72 (m, 2H, ArH), 7.36–7.28 (m, 2H, ArH), 6.01 (dd, $J=2.1$, 0.9 Hz, 1H, one proton in C=CH_2), 5.62 (d, $J=2.1$ Hz, 1H, one proton in C=CH_2), 5.18 (dd, $J=9.9$, 6.9 Hz, 1H, OCH), 4.25 (dd, $J=15.0$, 10.2 Hz, 1H, one proton in NCH_2), 4.02 (dd, $J=15.3$, 6.9 Hz, 1H, one proton in NCH_2), 2.39 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=163.3$, 137.9, 132.1, 131.4, 128.5, 128.1, 126.8, 125.1, 117.5, 81.0, 60.2, 21.0; IR (neat) $\nu=1645$, 1628, 1600, 1588, 1351, 1309, 1265, 1195, 1167, 1064, 1038 cm^{-1}; MS (EI): $m/z=267$ [M(^{81}Br)$^+$, 6.88], 265 [M(^{79}Br)$^+$, 7.06], 131 (100); anal. calcd. for $C_{12}H_{12}BrNO$: C 54.16, H 4.54, N 5.26; found: C 54.23, H 4.62, N 5.08.

5-(1-Bromovinyl)-2-(furan-2-yl)-4,5-dihydrooxazole (2k): The reaction of **1k** (164.1 mg, 1.0 mmol), NBS (214.5 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2k** as an oil (petroleum ether/ethyl acetate = 10:1 to 5:1); yield: 158.3 mg (65%); ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.57$ (d, $J=1.2$ Hz, 1H, furyl), 7.00 (d, $J=3.6$ Hz, 1H, furyl), 6.51 (dd, $J=3.4$, 1.6 Hz, 1H, furyl), 6.01 (dd, $J=1.8$, 0.9 Hz, 1H, one proton in C=CH_2), 5.64 (d, $J=1.8$ Hz, 1H, one proton in C=CH_2), 5.17 (dd, $J=10.0$, 7.0 Hz, 1H, OCH), 4.25 (dd, $J=15.2$, 10.0 Hz, 1H, one proton in NCH_2), 4.03 (dd, $J=15.0$, 6.9 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=155.6$, 145.4, 142.3, 130.8, 118.2, 114.6, 111.5, 81.4, 60.3; IR (neat): $\nu=1672$, 1480, 1402, 1341, 1167, 1092, 1007 cm^{-1}; MS (EI): $m/z=243$ [M(^{81}Br)$^+$, 9.93], 241 [M(^{79}Br)$^+$, 10.3], 107 (100); HR-MS: $m/z=240.9742$, calcd. for $C_9H_8{}^{79}BrNO_2$ [M$^+$]: 240.9738.

5-(1-Bromovinyl)-2-(thien-2-yl)-4,5-dihydrooxazole (2l): The reaction of **1l** (179.0 mg, 1.0 mmol), NBS (214.7 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2l** as an oil (petroleum ether/ethyl acetate = 10:1); yield: 176.1 mg (68%); ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.66$–7.62 (m, 1H, thienyl), 7.50–7.46 (m, 1H, thienyl), 7.12–7.06 (m, 1H, thienyl), 6.01 (dd, $J=2.1$, 0.9 Hz, 1H, one proton in C=CH_2), 5.63 (d, $J=1.8$ Hz, 1H, one proton in C=CH_2), 5.18 (dd, $J=9.8$, 7.0 Hz, 1H, OCH), 4.23 (dd, $J=15.0$, 9.9 Hz, 1H, one proton in NCH_2), 4.01 (dd, $J=15.2$, 6.8 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=159.0$, 131.0, 130.4, 130.1, 129.5, 127.5, 117.9, 81.6, 60.3; IR (neat): $\nu=1650$, 1524,

1431, 1336, 1252, 1200, 1078, 1052, 1007 cm^{-1}; MS (EI): m/z = 259 [M(^{81}Br)$^+$, 11.66], 257 [M(^{79}Br)$^+$, 11.39], 123 (100); HR-MS: m/z = 256.9511, calcd. for $C_9H_8{}^{79}BrNOS$ [M$^+$]: 256.9510.

5-(1-Bromovinyl)-2-(naphth-1-yl)-4,5-dihydrooxazole (2m): The reaction of **1m** (224.0 mg, 1.0 mmol), NBS (214.7 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2m** as a solid (petroleum ether/ethyl acetate = 10:1); yield: 228.9 mg (76%); mp 74–75 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.18 (d, J = 8.4 Hz, 1H, ArH), 8.13 (d, J = 7.2 Hz, 1H, ArH), 7.95 (d, J = 8.1 Hz, 1H, ArH), 7.86 (d, J = 8.4 Hz, 1H, ArH), 7.64–7.45 (m, 3H, ArH), 6.02 (s, 1H, one proton in C=CH_2), 5.63 (d, J = 1.8 Hz, 1H, one proton in C=CH_2), 5.18 (dd, J = 9.8, 7.4 Hz, 1H, OCH), 4.40 (dd, J = 15.2, 10.4 Hz, 1H, one proton in NCH_2), 4.19 (dd, J = 14.8, 7.1 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.0, 133.6, 132.1, 131.8, 131.0, 129.0, 128.4, 127.4, 126.2, 126.1, 124.6, 123.7, 118.0, 80.2, 61.2; IR (neat): ν = 1643, 1587, 1509, 1325, 1269, 1188, 1117, 1072 cm^{-1}; MS (EI): m/z = 303 [M(^{81}Br)$^+$, 17.98], 301 [M(^{79}Br)$^+$, 18.32], 167 (100); anal. calcd. for $C_{15}H_{12}BrNO$: C 59.62, H 4.00, N 4.64; found: C 59.43, H 3.98, N 4.50.

Gram-Scale Synthesis of 2m

To a flame-dried Schlenk tube were added **1m** (1.1186 g, 5.1 mmol), NBS (1.0688 g, 6.0 mmol), and CH_3CN (10 mL). After the reaction mixture had been stirred at room temperature for 45 min as monitored by TLC, it was quenched with a saturated aqueous solution of $NaHCO_3$ (2 mL) and $Na_2S_2O_3$ (2 mL). The resulting mixture was extracted with ether (30 mL × 3) and dried over anhydrous $MgSO_4$. After filtration and evaporation of the solvent, chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded **2m** as a solid; yield: 0.9801 g (67%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.18 (d, J = 8.4 Hz, 1H, ArH), 8.13 (d, J = 7.5 Hz, 1H, ArH), 7.94 (d, J = 8.4 Hz, 1H, ArH), 7.85 (d, J = 8.1 Hz, 1H, ArH), 7.64–7.44 (m, 3H, ArH), 6.00 (d, J = 0.9 Hz, 1H, one proton in C=CH_2), 5.62 (d, J = 1.8 Hz, 1H, one proton in C=CH_2), 5.16 (dd, J = 9.9, 7.2 Hz, 1H, OCH), 4.38 (dd, J = 15.3, 9.9 Hz, 1H, one proton in NCH_2), 4.18 (dd, J = 15.3, 6.9 Hz, 1H, one proton in NCH_2).

5-(1-Bromovinyl)-2-(naphth-2-yl)-4,5-dihydrooxazole (2n): The reaction of **1n** (223.9 mg, 1.0 mmol), NBS (214.3 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2n** as a solid (petroleum ether/ethyl acetate = 10:1); yield: 233.2 mg (78%); mp 123–124 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.47 (s, 1H, ArH), 8.05 (dd, J = 2.6, 1.7 Hz, 1H, ArH), 7.95–7.82 (m, 3H, ArH), 7.60–7.48 (m, 2H, ArH), 6.05 (dd, J = 1.8, 0.9 Hz, 1H, one proton in C=CH_2), 5.65 (d, J = 2.4 Hz, 1H, one proton in C=CH_2), 5.24 (dd, J = 9.9, 6.9 Hz, 1H, OCH), 4.31 (dd, J = 15.2, 10.1 Hz, 1H, one proton in NCH_2), 4.08 (dd, J = 15.2, 7.1 Hz, 1H, one proton in NCH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5, 134.7, 132.5, 131.5, 128.8, 128.7, 128.2, 127.7, 127.6, 126.5, 124.6, 124.3, 117.8, 81.3, 60.5; IR (neat): ν = 1644, 1588, 1510, 1326, 1269, 1189, 1118, 1073 cm^{-1}; MS (EI): m/z = 303 [M(^{81}Br)$^+$, 23.61], 301 [M(^{79}Br)$^+$, 23.95], 167 (100); anal. calcd. for $C_{15}H_{12}BrNO$: C 59.62, H 4.00, N 4.64; found: C 59.61, H 4.04, N 4.49.

5-(1-Bromovinyl)-2-butyl-4,5-dihydrooxazole (2o): The reaction of **1o** (152.9 mg, 1.0 mmol), NBS (213.6 mg, 1.2 mmol), and CH_3CN (4 mL) afforded **2o** as an oil (petroleum ether/ethyl acetate = 20:1 to 5:1); yield: 60.2 mg (26%); and an unknown side product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.94–5.91 (m, 1H, one proton in C=CH_2), 5.58 (d, J = 1.8 Hz, 1H, one proton in C=CH_2), 4.98 (dd, J = 10.0, 7.0 Hz, 1H, OCH), 4.01 (dd, J = 14.2, 10.0 Hz, 1H, one proton in NCH_2), 3.78 (dd, J = 14.4, 6.9 Hz, 1H, one proton in NCH_2), 2.32 (t, J = 7.8 Hz, 2H, CH_2), 1.65 (quint, J = 7.6 Hz, 2H, CH_2), 1.40 (sext, J = 7.4 Hz, 2H, CH_2), 0.93 (t, J = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.3, 131.8, 117.5, 80.8, 59.8, 27.8, 27.5, 22.2, 13.6; IR (neat): ν = 3364, 3267, 3093, 2954, 2932, 2871, 1632, 1608, 1565, 1464, 1421, 1379, 1326, 1231, 1071 cm^{-1}; MS (ESI): m/z = 234 [M(^{81}Br) + H$^+$], 232 [M(^{79}Br) + H$^+$]; HR-MS: m/z = 231.0258, calcd. for $C_9H_{14}{}^{79}BrNO$ [M$^+$]: 231.0259.

1,3-Bis[5-(1-bromovinyl)-4,5-dihydrooxazol-2-yl]benzene (2p): The reaction of **1p** (267.2 mg, 1.0 mmol), NBS (428.6 mg, 2.4 mmol), and CH_3CN (4 mL) afforded **2p** as a solid (petroleum ether/ethyl acetate = 3:1 to 1.5:1); yield: 230.7 mg (56%); mp 129–130 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.53 (dd, J = 3.5, 1.7 Hz, 1H, ArH), 8.12 (ddd, J = 7.7, 2.6, 1.8 Hz, 2H, ArH), 7.51 (t, J = 7.8 Hz, 1H, ArH), 6.02 (dd, J = 2.1, 0.9 Hz, 2H, one proton in C=CH_2), 5.64 (d, J = 2.4 Hz, 2H, one proton in C=CH_2), 5.21 (dd, J = 9.9, 7.2 Hz, 2H, OCH), 4.27 (dd, J = 15.3, 9.9 Hz, 2H, one proton in NCH_2), 4.05 (dd, J = 15.2, 7.0 Hz, 2H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.5, 131.2, 131.00, 130.97, 128.5, 127.8, 127.7, 127.4, 117.9, 81.4, 60.4; IR (neat): ν = 1653, 1358, 1337, 1280, 1231, 1207, 1160, 1061 cm^{-1}; MS (EI): m/z = 428 [M(^{81}Br,^{81}Br)$^+$, 6.39], 426 [M(^{81}Br,^{79}Br)$^+$, 12.52], 424 [M(^{79}Br,^{79}Br)$^+$, 6.41], 290 (100); anal. calcd. for $C_{16}H_{14}Br_2N_2O_2$: C 45.10, H 3.31, N 6.57; found: C 45.37, H 3.42, N 6.34.

Synthesis of 5-Ethynyl-2-phenyl-4,5-dihydrooxazole (3a); Typical Procedure II

To a dry Schlenk tube were added sequentially **2a** (252.5 mg, 1.0 mmol), TBAF·3H_2O (943.4 mg, 3.0 mmol), and DMF (4 mL). The resulting solution was stirred at 100 °C. When the reaction was complete as monitored by TLC, the mixture was filtered through a short pad of silica gel eluted with ether (50 mL). After evaporation, the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) to afford **3a** as an oil; yield: 140.2 mg (82%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98–7.93 (m, 2H, ArH), 7.52–7.37 (m, 3H, ArH), 5.24 (ddd, J = 9.9, 7.8, 1.8 Hz, 1H, OCH), 4.32 (dd, J = 14.4, 10.2 Hz, 1H, one proton in NCH_2), 4.11 (dd, J = 14.6, 7.6 Hz, 1H, one proton in NCH_2), 2.64 (d, J = 2.1 Hz, 1H, C≡CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 131.4, 128.2, 128.1, 126.9, 81.1, 75.3, 68.1, 61.9; IR (neat) ν = 1652, 1451, 1355, 1323, 1255, 1061, 1025 cm^{-1}; MS (EI): m/z = 171 (M$^+$, 19.58), 117 (100); HR-MS: m/z = 171.0683, calcd. for $C_{11}H_9NO$ [M$^+$]: 171.0684.

Products **3b** and **3c** were prepared according to Typical Procedure II.

5-Ethynyl-2-(4-methoxycarbonylphenyl)-4,5-dihydrooxazole (3b): The reaction of **2c** (312.1 mg, 1.0 mmol), TBAF·3H_2O (945.3 mg, 3.0 mmol), and DMF (4 mL) afforded **3b** as a solid (petroleum ether/ethyl acetate = 10:1 to 5:1); yield: 188.5 mg (82%); mp 112–114 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13–8.04 (m, 2H,

ArH), 8.04–7.98 (m, 2H, ArH), 5.28 (ddd, $J=10.2$, 7.8, 2.1 Hz, 1H, OCH), 4.35 (dd, $J=14.8$, 10.0 Hz, 1H, one proton in NCH_2), 4.12 (dd, $J=15.2$, 7.6 Hz, 1H, one proton in NCH_2), 3.92 (s, 3H, CH_3), 2.72 (d, $J=2.1$ Hz, 1H, C≡CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=166.1$, 162.3, 132.4, 130.9, 129.3, 128.1, 80.9, 75.6, 68.4, 62.1, 52.1; IR (neat): $\nu=$ 3247, 1707, 1651, 1286, 1116, 1065 cm^{-1}; MS (EI): $m/z=229$ (M^+, 13.83), 175 (100); anal. calcd. for $C_{13}H_{11}NO_3$: C 68.11, H 4.84, N 6.11; found: C 67.93, H 4.81, N 6.13.

5-Ethynyl-2-[4-(trifluoromethyl)phenyl]-4,5-dihydrooxazole (3c): The reaction of **2g** (321.5 mg, 1.0 mmol), TBAF·3 H_2O (949.5 mg, 3.0 mmol), and DMF (4 mL) afforded **3c** (petroleum ether/ethyl acetate = 10:1); yield: 139.4 mg (58%); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=8.06$ (d, $J=8.1$ Hz, 2H, ArH), 7.67 (d, $J=7.8$ Hz, 2H, ArH), 5.29 (ddd, $J=10.2$, 7.8, 2.1 Hz, 1H, OCH), 4.36 (dd, $J=14.8$, 10.0 Hz, 1H, one proton in NCH_2), 4.14 (dd, $J=14.7$, 7.8 Hz, 1H, one proton in NCH_2), 2.68 (d, $J=2.4$ Hz, 1H, C≡CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=162.1$, 133.1 (q, $J=32.5$ Hz), 130.4, 128.6, 125.3 (q, $J=3.8$ Hz), 123.7 (q, $J=270.8$ Hz), 80.9, 75.7, 68.6, 62.2; ^{19}F NMR ($CDCl_3$, 282 MHz): $\delta=-63.5$; IR (neat): $\nu=1656$, 1414, 1320, 1168, 1128, 1074, 1019 cm^{-1}; MS (EI): $m/z=239$ (M^+, 10.29), 185 (100); HR-MS: $m/z=$ 239.0561, calcd. for $C_{12}H_8F_3NO$ [M^+]: 239.0558.

Synthesis of 5-[1-(1*H*-indol-1-yl)vinyl]-2-phenyl-4,5-dihydrooxazole (4a); Typical Procedure III

CuI (38.5 mg, 0.2 mmol) and K_3PO_4 (423.7 mg, 2.0 mmol) were added to a screw-capped reaction tube with a Teflon-lined septum. The tube was evacuated and backfilled with argon three times. Then **2a** (252.2 mg, 1.0 mmol), indole (235.9 mg, 2.0 mmol), diethylamine (27.4 mg, 0.4 mmol), and 1,4-dioxane (1 mL) were added under an argon atmosphere. The reaction tube was sealed and the mixture was stirred at 130 °C for 48 h. When the reaction was completed, the mixture was filtered through a short pad of silica gel eluted with ethyl acetate (50 mL). After evaporation, the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 20:1 to 10:1 to 5:1) to afford **4a** as an oil; yield: 249.5 mg (86%); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$ 8.03–7.97 (m, 2H, ArH), 7.62 (d, $J=7.8$ Hz, 1H, ArH), 7.54–7.40 (m, 4H, ArH), 7.26–7.10 (m, 3H, ArH), 6.57 (d, $J=3.0$ Hz, 1H, ArH), 5.61 (s, 1H, one proton in C=CH_2), 5.51 (dd, $J=9.9$, 7.8 Hz, 1H, OCH), 5.49 (s, 1H, one proton in C=CH_2), 4.14 (dd, $J=14.8$, 10.0 Hz, 1H, one proton in NCH_2), 3.75 (dd, $J=15.0$, 7.5 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=163.4$, 142.7, 136.5, 131.6, 128.8, 128.4, 128.2, 127.2, 126.5, 122.5, 121.0, 120.4, 110.8, 110.6, 103.8, 79.1, 59.7; IR (neat): $\nu=1651$, 1456, 1320, 1214, 1060, 1026 cm^{-1}; MS (EI): $m/z=289$ (M^++1, 20.66), 288 (M^+, 100); HR-MS: $m/z=$ 288.1260, calcd. for $C_{19}H_{16}N_2O$ [M^+]: 288.1263.

Products **4b** and **4c** were prepared according to Typical Procedure III.

5-[1-(1*H*-Indol-1-yl)vinyl]-2-[4-(trifluoromethyl)phenyl]-4,5-dihydrooxazole (4b): The reaction of CuI (38.5 mg, 0.2 mmol), K_3PO_4 (423.1 mg, 2.0 mmol), **2g** (321.2 mg, 1.0 mmol), indole (234.3 mg, 2.0 mmol), diethylamine (28.9 mg, 0.4 mmol), and 1,4-dioxane (1 mL) afforded **4b** as an oil (petroleum ether/ethyl acetate = 10:1 to 5:1); yield: 233.2 mg (65%); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=8.07$ (d, $J=8.1$ Hz, 2H, ArH), 7.67 (d, $J=8.7$ Hz, 2H, ArH), 7.61 (d, $J=7.8$ Hz, 1H, ArH), 7.47 (d, $J=7.5$ Hz, 1H, ArH), 7.22 (td, $J=7.7$, 1.4 Hz, 1H, ArH), 7.17–7.10 (m, 2H, ArH), 6.56 (d, $J=2.7$ Hz, 1H, ArH), 5.58 (s, 1H, one proton in C=CH_2), 5.50 (dd, $J=10.1$, 8.0 Hz, 1H, OCH), 5.44 (s, 1H, one proton in C=CH_2), 4.13 (dd, $J=15.3$, 10.2 Hz, 1H, one proton in NCH_2), 3.76 (dd, $J=15.3$, 7.8 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=162.2$, 142.4, 136.5, 133.1 (q, $J=32.4$ Hz), 130.5, 128.8, 128.5, 126.4, 125.4 (q, $J=4.0$ Hz), 123.7 (q, $J=270.9$ Hz), 122.6, 121.0, 120.5, 111.3, 110.6, 104.0, 79.5, 59.7; ^{19}F NMR ($CDCl_3$, 282 MHz): $\delta=-63.4$; IR (neat): $\nu=1658$, 1455, 1320, 1162, 1132, 1074 cm^{-1}; MS (EI): $m/z=357$ (M^++1, 18.52), 356 (M^+, 78.56), 167 (100); HR-MS: $m/z=356.1131$, calcd. for $C_{20}H_{15}F_3N_2O$ [M^+]: 356.1136.

2-(3,5-Dichlorophenyl)-5-[1-(1*H*-indol-1-yl)vinyl]-4,5-dihydrooxazole (4c): The reaction of CuI (38.6 mg, 0.2 mmol), K_3PO_4 (423.1 mg, 2.0 mmol), **2e** (321.8 mg, 1.0 mmol), indole (233.1 mg, 2.0 mmol), diethylamine (31.0 mg, 0.4 mmol), and 1,4-dioxane (1 mL) afforded **4c** as an oil (petroleum ether/ethyl acetate = 20:1 to 10:1 for the first round, petroleum ether/ethyl acetate = 20:1 to 10:1 for the second round); yield: 281.2 mg (78%); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.85$ (d, $J=1.8$ Hz, 2H, ArH), 7.61 (d, $J=7.8$ Hz, 1H, ArH), 7.48–7.43 (m, 2H, ArH), 7.26–7.10 (m, 3H, ArH), 6.57 (dd, $J=3.3$, 0.6 Hz, 1H, ArH), 5.58 (s, 1H, one proton in C=CH_2), 5.50 (dd, $J=10.2$, 7.5 Hz, 1H, and OCH), 5.46 (s, 1H, one proton in C=CH_2) 4.12 (dd, $J=15.3$, 10.2 Hz, 1H, one proton in NCH_2), 3.72 (dd, $J=15.4$, 7.6 Hz, 1H, one proton in NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=161.2$, 142.2, 136.5, 135.2, 131.4, 130.0, 128.7, 126.5, 126.4, 122.6, 121.0, 120.5, 111.4, 110.5, 104.0, 79.7, 59.6; IR (neat): $\nu=1653$, 1563, 1456, 1313, 1256, 1214, 1088 cm^{-1}; MS (EI): $m/z=360$ [$M(^{37}Cl,^{37}Cl)^+$, 4.66], 358 [$M(^{37}Cl,^{35}Cl)^+$, 26.41], 356 [$M(^{35}Cl,^{35}Cl)^+$, 39.91], 167 (100); HR-MS: $m/z=356.0484$, calcd. for $C_{19}H_{14}{}^{35,35}Cl_2N_2O$ [M^+]: 356.0483.

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