有机化学 DOI: 10.6023/cjoc202005064 研究论文
Chinese Journal of Organic Chemistry ARTICLE

铜参与的烯基酰胺 β-碳氢键与端炔的炔基化反应

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摘要 基于噁唑啉酰胺导向基团实现了铜参与的烯基酰胺β-碳氢键与端炔的炔基化反应, 构建了一系列 1,3-共轭烯炔化合物. 该反应条件温和, 底物适用范围广, 具有良好的区域及立体选择性.
关键词 β-碳氢键炔基化; 铜; 1,3-烯炔; 立体选择性

Cu(II)-Mediated β-C—H Alkynylation of Acrylamides with Terminal Alkynes

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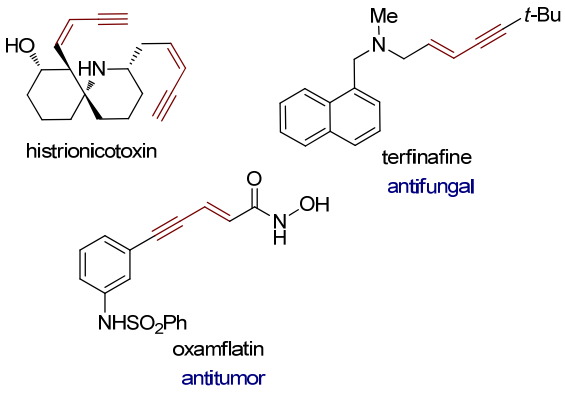
Abstract Cu(II)-mediated β-C—H alkynylation of acrylamides with terminal alkynes is described by employing amide-oxazoline bidentate auxiliary, forming the conjugated 1,3-enynes. This protocol is characterized by its mild conditions, broad substarate scope and excellent regio- and stereo-selectivity.
Keywords β-C—H alkynylation; copper; 1,3-enynes; stereo-selectivity

1 Introduction

1,3-Enynes are important structural motifs and prevalent in nature product, pharmaceuticals and functional materials.[1] For example, histrionicotoxin is toxins isolated from the poison-arrow frog *Dendrobates histrionicus*,[2] while terfinafine[3] and oxamflatin[4] are important pharmaceutically molecules (Scheme 1). 1,3-Enynes are not only present in a range of compounds with functional significance, but also been employed as versatile building block in organic synthesis.[5] Thus the development of an efficient and practical synthetic methodologies for the construction of 1,3-enynes has been an important objective.

In the past few decades, the transition-metal-catalyzed cross-coupling reactions were well documented for the preparation of 1,3-enyne moieties.[6] Particularly, the Pd and Cu co-catalyzed Sonogashira coupling of vinyl halides



Scheme 1 1,3-Enynes containing drug molecules

with terminal alkynes has been extensively studied and practiced in both academic and industrial settings (Scheme 2a).[7] Recently, with the rapid development of transi-

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Received May 23, 2020; revised June 20, 2020; published online July 8, 2020.
Dedicated to Professor Henry N. C. Wong on the occasion of his 70th birthday.
Project supported by the National Natural Science Foundation of China (No. 21772211), the Youth Innovation Promotion Association CAS (Nos. 2014229, 2018293), and the Science and Technology Commission of Shanghai Municipality (No. 17JC1405000).
国家自然科学基金(No. 21772211)、中国科学院青年创新促进会(Nos. 2014229, 2018293)、上海市科委(No. 17JC1405000)资助项目.

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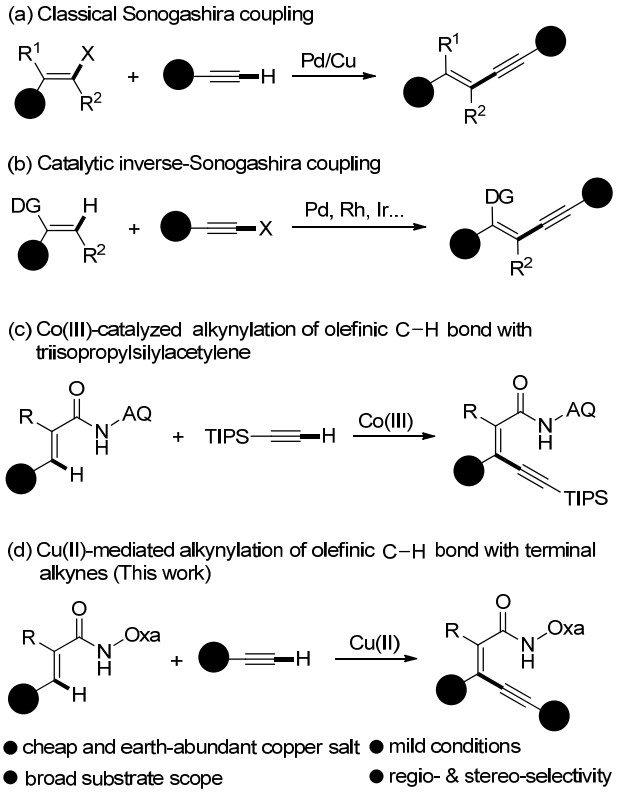
tion-metal-catalyzed C—H functionalization, direct C—H alkynylation with alkyne reagents has received more and more attentions (Scheme 2b).[8] Despite the elegant advances, noble metal catalysts (Pd, Rh, Ir), preactivated vinyl halides or alkynylating reagents such as hypervalent iodine reagents are often required in the reaction.[9] Direct cross dehydrogenlative alkynylation of simple alkenes with alkynes could avoid prefunctionalization, thus enabling construction of 1,3-enyne skeletons rapidly. To the best of our knowledge, this catalytic oxidative C—H/C—H coupling of alkenes with alkynes has been rarely reported in contrast with the alkynylation of arenes.[10-11] In 2019, with the assistance of 8-aminoquinoline (AQ) directing group, You *et al.*[11a] reported Co(III)-catalyzed oxidative C—H/C—H cross-coupling reaction of acrylamides with triisopropylsilylacetylene (Scheme 2c).



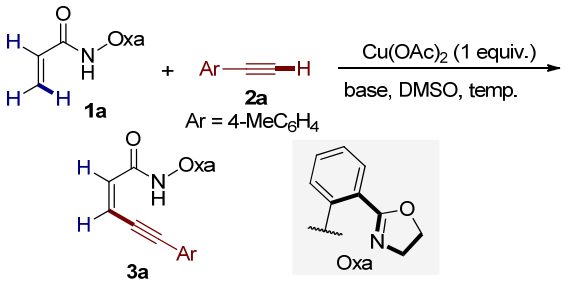
Scheme 2 Construction of conjugated enynes via C—H alkynylation

Based on our previous work on Cu-catalyzed C—H functionalization,[12-13] we questioned whether we could regio- and stereo-selectively construct 1,3-enyne compounds via Cu-catalyzed or mediated olefinic C—H alkynylation with readily accessible terminal alkynes. Herein, we described a Cu(II)-mediated *β*-selective C—H alkynylation of acrylamides with terminal alkynes by employing amide-oxazoline bidentate auxiliary (Scheme 2d). Our protocol is characterized by its mild conditions, good functional group tolerance and regio- and stereo-selectivity, thus enabling to access a variety of densely functionalized *cis*-enynes.

2 Results and discussion

Promoted by our previous work on Cu-mediated *ortho* C—H alkynylation of arenes,[14] our investigations were commenced by using acrylamide **1a** with *p*-tolylacetylene (**2a**) as the starting material. By employing amide-oxazoline as directing group, direct *β*-C—H alkynylation of acrylamide **1a** with **2a** (3 equiv.) could proceed in the presence of 1 equiv. of $Cu(OAc)_2$, providing *cis*-enyne **3a** in 28% yield (Table 1, Entry 1). Homo-coupling product 1,3-diynes were determined as the major byproduct. Next, the influence of bases was screened, and it was found that NaOAc provided the best result (Table 1, Entries 1～5). The yield could be improved to 39% when the reaction temperature was elevated to 80 ℃ (Table 1, Entries 6, 7). When the amount of NaOAc was increased to 3 equiv., 56% yield of desired product was obtained (Table 1, Entry 8). Increasing the reaction time did not improve the yields (Table 1, Entries 8～10). It is worth noting that no desired product was observed in the absence of copper, indicating that the copper is indispensable in the reaction (Table 1, Entry 11). Decreasing the loading of $Cu(OAc)_2$ to 20 mol% lead to the decreased yields (Table 1, Entry 12). For further investigation on the effect of the directing group, a variety of sterically diverse oxazoline groups were screened and it was found that oxazoline (Oxa) was the optimal choice (see the Supporting Information).

Table 1 Screening of the reaction conditions[a]



Entry	Base	*T*/℃	Time/h	Yield/%
1	NaOAc	60	6	28
2	LiOAc	60	6	24
3	KOAc	60	6	25
4	Na_2CO_3	60	6	20
5	K_2CO_3	60	6	17
6	NaOAc	80	6	39
7	NaOAc	100	6	30
8[c]	NaOAc	80	6	56
9[c]	NaOAc	80	4	51
10[c]	NaOAc	80	9	56
11[c,d]	NaOAc	80	6	0
12[c,e]	NaOAc	80	6	16

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), **2a** (0.3 mmol, 3.0 equiv.), $Cu(OAc)_2$ (0.1 mmol, 1.0 equiv.), base (0.2 mmol, 1.0 equiv.), DMSO (5.0 mL), air. [b] Yield was determined by ^1H NMR analysis of crude reaction mixture using CH_2Br_2 as an internal standard. [c] NaOAc (0.3 mmol). [d] No $Cu(OAc)_2$. [e] 20 mol% $Cu(OAc)_2$.

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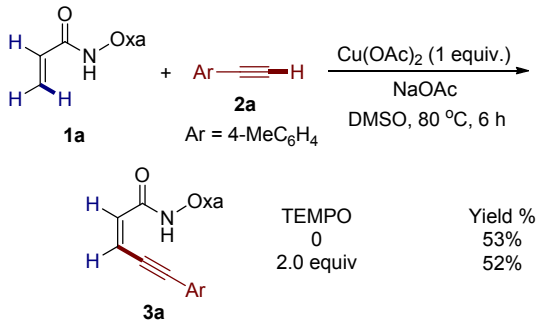
With the optimized reaction conditions in hand, we turned our attention to explore the generality of terminal alkynes. As shown in Table 3, a variety of functionalized aryl acetylenes with both electron-rich (**3a**～**3d**) and electron-deficient substituents (**3e**～**3j**) were tolerated. Notably, the halogen-containing substrates (**3e**～**3i**) were well tolerant, leaving a handle for further functionalization *via* metal-catalyzed cross-coupling reactions. Alkyne bearing heterocycle (**2k**) was also compatible, providing the product **3k** in 40% yield. Aliphatic alkynes were well employed in the reaction, furnishing the desired *cis*-1,3-enynes product in moderate yields (**3l**～**3n**). Next, we screened various substituents at both *α*- and *β*-position of acrylamides. To our delight, *cis*-1,3-enyne products could be obtained in moderate to good yield, regardless of the aliphatic (**3o**, **3q**, **3r**) or aryl (**3p**, **3s**～**3v**) groups. Noteworthy, cyclic acrylamides (**3w**, **3x**) could proceed smoothly, giving the tetrasubstituted *cis*-1,3-enyne products in moderate yields.

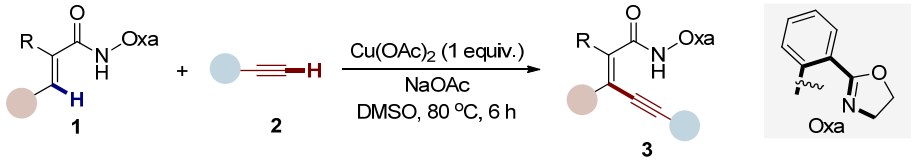
To probe the reaction mechanism, 2 equiv. of radical scavengers 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) were added in the reaction. 52% yield of product **3a** was obtained, indicating that a radical pathway might not involve in the reaction (Scheme 3).

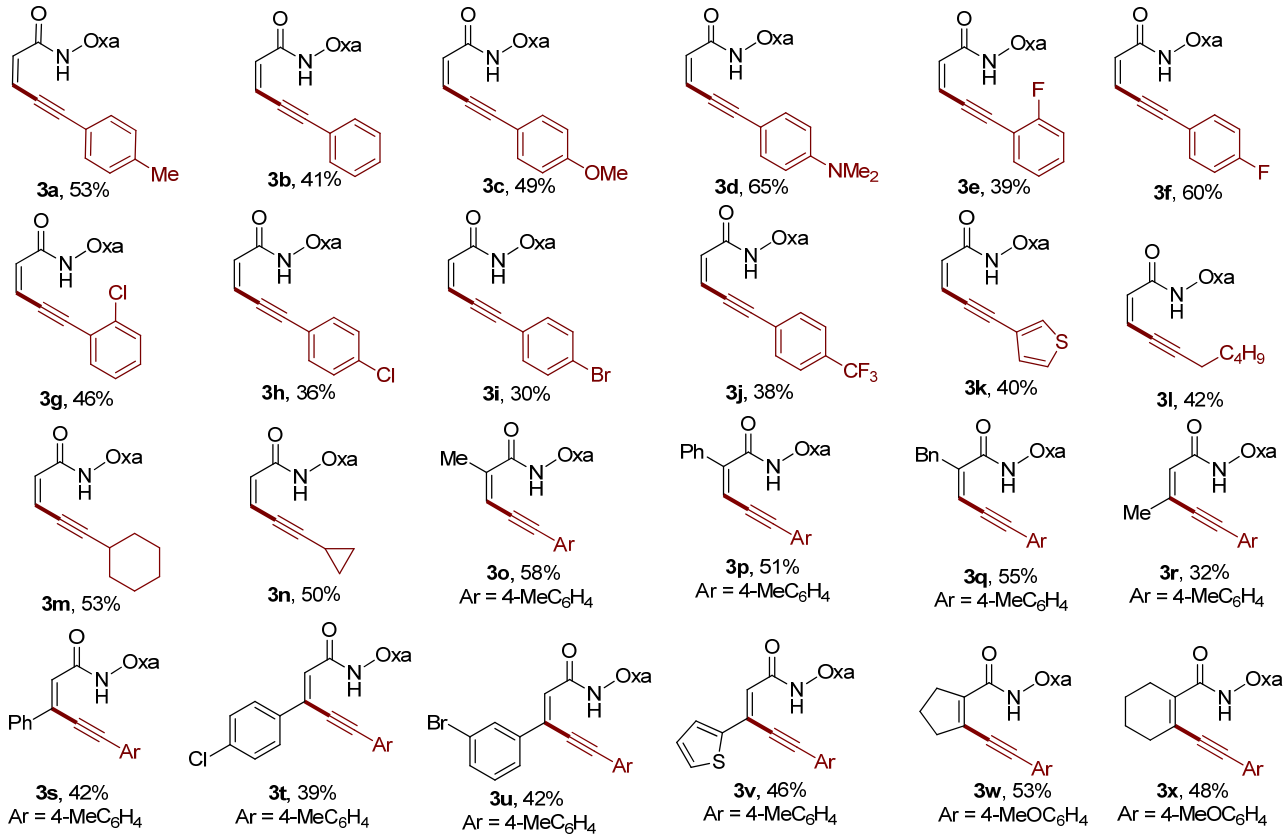


Scheme 3 The effect of TEMPO

Based on the control experiment and previous reports,[15] we proposed a possible mechanism on copper(II)-mediated C—H alkynylation of acrylamides (Scheme 4). Oxazo line-

Table 2 Substrate scope for the reaction[a]





[a] Reaction conditions: **1** (0.1 mmol, 1.0 equiv.), **2** (0.3 mmol, 3.0 equiv.), $Cu(OAc)_2$ (0.1mmol, 1.0 equiv.), NaOAc (0.3 mmol, 3.0 equiv.), DMSO (5.0 mL), air, at 80 ℃ for 6 h.

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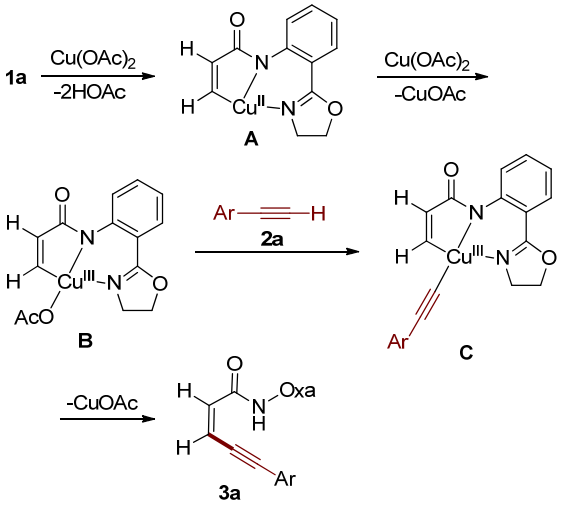
directed C—H activation of **1a** with $Cu(OAc)_2$ formed the Cu(II) intermediate **A**, which then underwent disproportionation of copper(II) with $Cu(OAc)_2$ yielded Cu(III) complex **B**. Transmetallation of terminal alkyne with complex **B** formed the intermediate **C**, which subsequently underwent reductive elimination to release the *cis*-1,3-enynesproduct **3a** and Cu(I) species.



Scheme 4 Plausible pathway

3 Conclusions

In conclusion, we have documented a Cu(II)-mediated *β*-selective C—H alkynylation of acrylamides by employing amide-oxazoline as the directing group. Stereospecific *cis*-1,3-enynes products were obtained in moderate to good yield. The reaction condition is mild, and a variety of (hetero)aryl and alkyl group at both *α*- and *β*-position of acrylamides could be well tolerated.

4 Experimental section

4.1 General procedure for the synthesis of 1

To a stirred solution of Et_3N (7.5 mmol) and 2-(4,5-dihydrooxazol-2-yl)aniline (5 mmol) in CH_2Cl_2 (15 mL) was added acyl chloride (5 mmol) dropwise at 0 ℃. Then the reaction mixture was stirred at room temperature for 6 h. Upon completion, EtOAc was added to dilute the mixture and washed with saturated $NaHCO_3$ (aq.). The organic fraction was dried over anhydrous Na_2SO_4. Then, the solvent was evaporated, and the crude product was purified by flash column chromatography with petroleum ether/ethyl acetate as the eluent.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)acrylamide (**1a**): White solid, m.p. 97～98 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 12.46 (s, 1H), 8.83 (d, *J*=8.4 Hz, 1H), 7.86 (dd, *J*=8.0, 1.6 Hz, 1H), 7.47 (t, *J*=7.1 Hz, 1H), 7.08 (t, *J*=7.6 Hz, 1H), 6.42 (dd, *J*=17.1, 1.2 Hz, 1H), 6.31 (dd, *J*=17.1, 10.2 Hz, 1H), 5.75 (dd, *J*=10.2, 1.2 Hz, 1H), 4.38 (t, *J*=9.5 Hz, 2H), 4.14 (t, *J*=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 164.75, 164.38, 139.86 , 132.80, 132.53, 129.17, 126.64, 122.40, 119.82, 113.26, 66.16, 54.65; HRMS (ESI-TOF) calcd for $C_{12}H_{13}N_2O_2$ $[M+H]^+$ 217.0972, found 217.0974.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)methacrylamide (**1b**): White solid, m.p. 72～73 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 12.52 (s, 1H), 8.84 (dd, *J*=8.5, 1.1 Hz, 1H), 7.86 (dd, *J*=7.8, 1.6 Hz, 1H), 7.47 (ddd, *J*=8.8, 7.4, 1.7 Hz, 1H), 7.07 (td, *J*=7.6, 1.1 Hz, 1H), 6.01 (s, 1H), 5.50 (s, 1H), 4.37 (t, *J*=9.5 Hz, 2H), 4.13 (t, *J*=9.4 Hz, 2H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 168.16, 165.72, 142.07, 141.00, 133.49, 130.17, 123.20, 121.86, 120.73, 114.40, 67.15, 55.63, 19.75; HRMS (ESI-TOF) calcd for $C_{13}H_{15}N_2O_2$ $[M+H]^+$ 231.1128, found 231.1131.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-2-phenylacrylamide (**1c**): White solid, m.p. 95～97 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 12.37 (s, 1H), 8.94 (d, *J*=8.4 Hz, 1H), 7.81 (d, *J*=7.2 Hz, 1H), 7.54～7.42 (m, 3H), 7.41～7.37 (m, 3H), 7.08 (t, *J*=7.6 Hz, 1H), 6.29 (d, *J*=1.1 Hz, 1H), 5.73 (d, *J*=1.1 Hz, 1H), 4.22 (t, *J*=9.5 Hz, 2H), 3.67 (t, *J*=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 166.61, 164.04, 146.42, 139.83, 137.13, 132.36, 128.99, 128.82, 128.16, 128.13, 122.67, 122.44, 119.80, 113.55, 66.05, 54.26; HRMS (ESI-TOF) calcd for $C_{18}H_{17}N_2O_2$ $[M+H]^+$ 293.1285, found 293.1284.

2-Benzyl-*N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)acrylamide (**1d**): White solid, m.p. 83～85 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 12.63 (s, 1H), 8.84 (d, *J*=8.5 Hz, 1H), 7.86 (dd, *J*=8.0, 1.6 Hz, 1H), 7.46 (t, *J*=7.9 Hz, 1H), 7.35～7.25 (m, 4H), 7.22 (t, *J*=7.0 Hz, 1H), 7.07 (t, *J*=7.7 Hz, 1H), 6.10 (s, 1H), 5.39 (s, 1H), 4.36 (t, *J*=9.5 Hz, 2H), 4.11 (t, *J*=9.5 Hz, 2H), 3.81 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 166.78, 164.68, 145.35, 139.92, 138.88, 132.46, 129.15, 129.10, 128.37, 126.21, 122.20, 121.02, 119.69, 113.33, 66.11, 54.60, 38.11; HRMS (ESI-TOF) calcd for $C_{19}H_{19}N_2O_2$ $[M+H]^+$ 307.1441, found 307.1446.

(*E*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)but-2-enamide (**1e**): White solid, m.p. 122～124 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 12.25 (s, 1H), 8.82 (dd, *J*=8.5, 1.1 Hz, 1H), 7.84 (dd, *J*=7.9, 1.7 Hz, 1H), 7.45 (ddd, *J*=8.7, 7.3, 1.7 Hz, 1H), 7.05 (td, *J*=7.6, 1.2 Hz, 1H), 7.01～6.94 (m, 1H), 6.02 (dd, *J*=15.2, 1.7 Hz, 1H), 4.39 (t, *J*=9.3 Hz, 2H), 4.14 (t, *J*=9.3 Hz, 2H), 1.92 (dd, *J*=6.9, 1.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 164.74, 164.69, 140.10, 132.44, 129.11, 126.90, 122.05, 119.74, 113.06, 66.08, 54.68, 17.81; HRMS (ESI-TOF) calcd for $C_{13}H_{15}N_2O_2$ $[M+H]^+$ 231.1128, found 231.1128.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)cinnamamide (**1f**): White solid, m.p. 146～149 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 12.51 (s, 1H), 8.90 (dd, *J*=8.4, 1.1 Hz, 1H), 7.87 (dd, *J*=8.0, 1.5 Hz, 1H), 7.76 (d, *J*=15.6 Hz, 1H), 7.58 (d, *J*=6.1 Hz, 2H), 7.49 (t, *J*=7.1 Hz, 1H), 7.38 (q, *J*=8.4, 7.4 Hz, 3H), 7.08 (t, *J*=7.6 Hz, 1H), 6.60 (d, *J*=15.6 Hz, 1H), 4.38 (t, *J*=9.5 Hz, 2H), 4.18 (t, *J*=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 164.73, 164.67, 141.44, 140.06, 134.86, 132.47, 129.70, 129.17, 128.74, 127.91, 122.50, 122.25, 119.80, 113.12, 66.10, 54.70; HRMS (ESI-TOF) calcd for $C_{18}H_{17}N_2O_2$ $[M+H]^+$ 293.1285, found 293.1286.

(*E*)-3-(4-Chlorophenyl)-*N*-(2-(4,5-dihydrooxazol-2-yl)-phenyl)acrylamide (**1g**): White solid, m.p. 161～164 ℃; ^{1}H

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NMR (500 MHz, $CDCl_3$) δ: 12.51 (s, 1H), 8.88 (dd, J=8.4, 1.1 Hz, 1H), 7.87 (dd, J=7.9, 1.6 Hz, 1H), 7.69 (d, J=15.6 Hz, 1H), 7.49 (t, J=9.3 Hz, 3H), 7.35 (d, J=8.5 Hz, 2H), 7.09 (td, J=7.6, 1.2 Hz, 1H), 6.56 (d, J=15.6 Hz, 1H), 4.40 (t, J=9.8 Hz, 2H), 4.19 (t, J=9.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.80, 164.36, 140.12, 139.98, 135.54, 133.38, 132.57, 129.21, 129.13, 129.02, 123.00, 122.42, 119.87, 113.17, 66.16, 54.74; HRMS (ESI-TOF) calcd for $C_{18}H_{16}ClN_2O_2$ $[M+H]^+$ 327.0895, found 327.0899.

(*E*)-3-(3-Bromophenyl)-*N*-(2-(4,5-dihydrooxazol-2-yl)-phenyl)acrylamide (**1h**): White solid, m.p. 143～145 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.54 (s, 1H), 8.87 (dd, J=8.5, 1.1 Hz, 1H), 7.88 (dd, J=7.9, 1.7 Hz, 1H), 7.73 (t, J=1.8 Hz, 1H), 7.66 (d, J=15.6 Hz, 1H), 7.53～7.45 (m, 3H), 7.26 (t, J=7.9 Hz, 1H), 7.10 (td, J=7.6, 1.2 Hz, 1H), 6.58 (d, J=15.6 Hz, 1H), 4.41 (t, J=9.8 Hz, 2H), 4.22 (t, J=9.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.79, 164.13, 139.92, 139.89, 137.04, 132.57, 132.50, 130.37, 130.30, 129.23, 126.84, 123.87, 122.90, 122.50, 119.91, 113.24, 66.19, 54.78; HRMS (ESI-TOF) calcd for $C_{18}H_{16}BrN_2O_2$ $[M+H]^+$ 371.0390, found 371.0394.

(*E*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-3-(thiophen-2-yl)acrylamide (**1i**): White solid, m.p. 114～116 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.44 (s, 1H), 8.87 (dd, J=8.4, 1.2 Hz, 1H), 7.88 (dd, J=7.9, 1.7 Hz, 1H), 7.87 (d, J=15.3 Hz, 1H), 7.49 (ddd, J=8.7, 7.3, 1.7 Hz, 1H), 7.35 (d, J=5.0 Hz, 1H), 7.28 (d, J=3.7 Hz, 1H), 7.09 (td, J=7.7, 1.2 Hz, 1H), 7.06 (dd, J=5.1, 3.6 Hz, 1H), 6.41 (d, J=15.3 Hz, 1H), 4.40 (t, J=9.2 Hz, 2H), 4.21 (t, J=9.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.76, 164.47, 140.07, 140.04, 134.18, 132.54, 130.35, 129.19, 128.00, 127.54, 122.30, 121.32, 119.89, 113.14, 66.17, 54.76; HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_2S$ $[M+H]^+$ 299.0849, found 299.0853.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)cyclopent-1-ene-1-carboxamide (**1j**): White solid, m.p. 127～129 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.38 (s, 1H), 8.85 (dd, J=8.4, 1.1 Hz, 1H), 7.85 (dt, J=7.9, 1.8 Hz, 1H), 7.46 (td, J=8.6, 7.9, 1.6 Hz, 1H), 7.05 (td, J=7.6, 1.3 Hz, 1H), 6.77 (tt, J=2.7, 1.6 Hz, 1H), 4.38 (td, J=9.4, 2.1 Hz, 2H), 4.15 (td, J=9.2, 2.2 Hz, 2H), 2.75～2.70 (m, 2H), 2.58～2.53 (m, 2H), 2.06～2.00 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.73, 164.45, 141.08, 140.15, 139.27, 132.50, 129.14, 121.97, 119.67, 113.09, 66.12, 54.66, 33.40, 31.44, 23.33; HRMS (ESI-TOF) calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$ 257.1285, found 257.1285.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)cyclohex-1-ene-1-carboxamide (**1k**): White solid, m.p. 126～128 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.28 (s, 1H), 8.85 (d, J=8.5 Hz, 1H), 7.85 (dd, J=7.9, 1.6 Hz, 1H), 7.45 (t, J=7.9 Hz, 1H), 7.04 (t, J=7.6 Hz, 1H), 6.90 (tt, J=3.8, 1.7 Hz, 1H), 4.36 (t, J=9.5 Hz, 2H), 4.13 (t, J=9.5 Hz, 2H), 2.44～2.40 (m, 2H), 2.26～2.22 (m, 2H), 1.76～1.70 (m, 2H), 1.68～1.61 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.54, 164.70, 140.29, 135.04, 134.47, 132.42, 129.12, 121.85, 119.85, 113.29, 66.09, 54.67, 25.76, 24.28, 22.30, 21.58; HRMS (ESI-TOF) calcd for $C_{16}H_{19}N_2O_2$ $[M+H]^+$ 271.1441, found 271.1445.

4.2 General procedure for the synthesis of 3

To a 15 mL sealed tube was added acrylamides **1** (0.1 mmol, 1.0 equiv.), $Cu(OAc)_2$ (0.1 mmol, 18.1 mg, 1.0 equiv.), NaOAc (0.3 mmol, 24.6 mg, 3.0 equiv.), DMSO (5 mL), and alkynes **2** (0.3 mmol, 3.0 equiv.). The reaction vessel was placed into a pre-heated oil bath at 80 ℃ for 6 h. Upon completion, EtOAc was added to dilute the mixture, then washed with NH_3•H_2O and saturated aq. NaCl. The organic fraction was dried over anhydrous Na_2SO_4, and then concentrated under reduced pressure. The residue was purified through silica gel packed flash chromatography column using ethyl acetate/hexane as the eluent.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-(*p*-tolyl)-pent-2-en-4-ynamide (**3a**): 17.4 mg, 53% yield. White solid, m.p. 68～70 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.56 (s, 1H), 8.90 (dd, J=8.5, 1.1 Hz, 1H), 7.86 (dd, J=7.9, 1.7 Hz, 1H), 7.48 (ddd, J=8.8, 7.4, 1.7 Hz, 1H), 7.36 (d, J=8.1 Hz, 2H), 7.14～7.06 (m, 3H), 6.28 (s, 2H), 4.23 (t, J=9.5 Hz, 2H), 4.00 (t, J=9.5 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.36, 163.33, 139.70, 139.23, 132.76, 132.43, 131.89, 129.10, 129.03, 122.43, 120.07, 119.75, 118.83, 113.35, 100.41, 86.09, 66.09, 54.61, 21.52; HRMS (ESI-TOF) calcd for $C_{21}H_{19}N_2O_2$ $[M+H]^+$ 331.1441, found 331.1441.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-phenylpent-2-en-4-ynamide (**3b**): 12.9 mg, 41% yield. White solid, m.p. 116～118 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.57 (s, 1H), 8.90 (dd, J=8.5, 1.1 Hz, 1H), 7.86 (dd, J=7.9, 1.6 Hz, 1H), 7.52～7.44 (m, 3H), 7.35～7.26 (m, 3H), 7.10 (td, J=7.6, 1.2 Hz, 1H), 6.32 (d, J=11.5 Hz, 1H), 6.28 (d, J=11.5 Hz, 1H), 4.24 (t, J=9.5 Hz, 2H), 4.02 (t, J=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.44, 163.26, 139.70, 133.29, 132.49, 131.96, 129.14, 128.92, 128.27, 122.85, 122.51, 120.12, 118.68, 113.38, 99.99, 86.55, 66.12, 54.63; HRMS (ESI-TOF) calcd for $C_{20}H_{17}N_2O_2$ $[M+H]^+$ 317.1285, found 317.1286.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-(4-methoxyphenyl)pent-2-en-4-ynamide (**3c**): 17.0 mg, 49% yield. White solid, m.p. 95～97 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.54 (s, 1H), 8.90 (d, J=8.7 Hz, 1H), 7.85 (dd, J=8.0, 1.6 Hz, 1H), 7.48 (t, J=7.2 Hz, 1H), 7.41 (d, J=8.7 Hz, 2H), 7.08 (t, J=7.4 Hz, 1H), 6.82 (d, J=8.6 Hz, 2H), 6.28 (d, J=11.5 Hz, 1H), 6.24 (d, J=11.5 Hz, 1H), 4.23 (t, J=9.5 Hz, 2H), 4.00 (t, J=9.5 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.34, 163.39, 160.19, 139.73, 133.59, 132.40, 132.14, 129.10, 122.38, 120.04, 119.03, 114.90, 113.92, 113.31, 100.54, 85.81, 66.09, 55.23, 54.60; HRMS (ESI-TOF) calcd for $C_{21}H_{19}N_2O_3$ $[M+H]^+$ 347.1390, found 347.1391.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-(4-(dimethylamino)phenyl)pent-2-en-4-ynamide (**3d**): 23.4 mg, 65% yield. Yellow solid, m.p. 132～135 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.51 (s, 1H), 8.90 (d, J=8.5 Hz, 1H), 7.86 (dd, J=7.9, 1.6 Hz, 1H), 7.48 (t, J=7.7 Hz, 1H), 7.33 (d, J=8.7 Hz, 2H), 7.08 (t, J=7.6 Hz, 1H), 6.59 (d, J=8.8 Hz,

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2H), 6.29 (d, J=11.5 Hz, 1H), 6.17 (d, J=11.5 Hz, 1H), 4.22 (t, J=9.5 Hz, 2H), 3.99 (t, J=9.5 Hz, 2H), 2.97 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.26, 163.80, 150.55, 139.88, 133.43, 132.36, 130.70, 129.09, 122.24, 120.16, 119.26, 113.38, 111.54, 109.36, 102.58, 85.76, 66.13, 54.66, 40.03; HRMS (ESI-TOF) calcd for $C_{22}H_{22}N_3O_2$ $[M+H]^+$ 360.1707, found 360.1701.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-(2-fluorophenyl)pent-2-en-4-ynamide (**3e**): 13.0 mg, 39% yield. White solid, m.p. 114～116 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.57 (s, 1H), 8.89 (dd, J=8.4, 1.1 Hz, 1H), 7.86 (dd, J=7.9, 1.6 Hz, 1H), 7.52～7.44 (m, 2H), 7.33～7.29 (m, 1H), 7.13～7.02 (m, 3H), 6.35 (d, J=11.5 Hz, 1H), 6.32 (d, J=11.5 Hz, 1H), 4.28 (t, J=9.5 Hz, 2H), 4.05 (t, J=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.51, 163.01, 162.68 (d, J=252.8 Hz), 139.68, 133.95, 133.80, 132.48, 130.74, 130.68, 129.11, 123.95 (d, J=3.8 Hz), 122.54, 120.12, 115.47 (d, J=20.9 Hz), 113.39, 111.59 (d, J=15.5 Hz), 93.09, 91.25 (d, J=3.4 Hz), 66.14, 54.63; ^{19}F NMR (471 MHz, $CDCl_3$) δ: －108.99 (m); HRMS (ESI-TOF) calcd for $C_{20}H_{16}FN_2O_2$ $[M+H]^+$ 335.1190, found 335.1192.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-(4-fluorophenyl)pent-2-en-4-ynamide (**3f**): 20.0 mg, 60% yield. White solid, m.p. 142～145 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.54 (s, 1H), 8.89 (d, J=8.4 Hz, 1H), 7.86 (dd, J=8.0, 1.7 Hz, 1H), 7.48 (dt, J=8.7, 6.3 Hz, 3H), 7.10 (td, J=7.7, 1.1 Hz, 1H), 7.01 (t, J=8.7 Hz, 2H), 6.31 (d, J=11.5 Hz, 1H), 6.26 (d, J=11.5 Hz, 1H), 4.29 (t, J=9.5 Hz, 2H), 4.04 (t, J=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.52, 163.12, 162.90 (d, J=250.2 Hz), 139.70, 133.99 (d, J=8.6 Hz), 133.18, 132.52, 129.16, 122.55, 120.07, 119.02 (d, J=3.0 Hz), 118.83, 115.63 (d, J=22.0 Hz), 113.32, 98.97, 86.45 (d, J=1.3 Hz), 66.14, 54.63; ^{19}F NMR (471 MHz, $CDCl_3$) δ: －109.63 (t, J=7.1 Hz); HRMS (ESI-TOF) calcd for $C_{20}H_{16}FN_2O_2$ $[M+H]^+$ 335.1190, found 335.1192.

(*Z*)-5-(2-Chlorophenyl)-*N*-(2-(4,5-dihydrooxazol-2-yl)-phenyl)pent-2-en-4-ynamide (**3g**): 16.1 mg, 46% yield. White solid, m.p. 92～94 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.57 (s, 1H), 8.88 (dd, J=8.5, 1.1 Hz, 1H), 7.85 (dd, J=7.9, 1.6 Hz, 1H), 7.52 (dd, J=7.6, 1.8 Hz, 1H), 7.48 (ddd, J=8.7, 7.4, 1.7 Hz, 1H), 7.38 (dd, J=7.9, 1.3 Hz, 1H), 7.25 (td, J=7.7, 1.8 Hz, 1H), 7.20 (td, J=7.5, 1.3 Hz, 1H), 7.10 (td, J=7.6, 1.2 Hz, 1H), 6.37 (d, J=11.5 Hz, 1H), 6.34 (d, J=11.5 Hz, 1H), 4.26 (t, J=9.4 Hz, 2H), 4.04 (t, J=9.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.48, 163.07, 139.68 , 136.04, 134.02, 133.98, 132.47, 129.88, 129.23, 129.11, 126.40, 122.90, 122.56, 120.11, 118.27, 113.45, 96.23, 91.14, 66.14, 54.64; HRMS (ESI-TOF) calcd for $C_{20}H_{16}ClN_2O_2$ $[M+H]^+$ 351.0895, found 351.0896.

(*Z*)-5-(4-Chlorophenyl)-*N*-(2-(4,5-dihydrooxazol-2-yl)-phenyl)pent-2-en-4-ynamide (**3h**): 12.6 mg, 36% yield. White solid, m.p. 129～132 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.56 (s, 1H), 8.88 (dd, J=8.5, 1.1 Hz, 1H), 7.86 (dd, J=7.9, 1.7 Hz, 1H), 7.48 (ddd, J=8.7, 7.4, 1.7 Hz, 1H), 7.43～7.40 (m, 2H), 7.31～7.27 (m, 2H), 7.10 (td, J=7.6, 1.1 Hz, 1H), 6.33 (d, J=11.5 Hz, 1H), 6.27 (d, J=11.5 Hz, 1H), 4.29 (t, J=9.5 Hz, 2H), 4.04 (t, J=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.50, 163.02, 139.63, 135.00, 133.49, 133.17, 132.52, 129.16, 128.64, 122.58, 121.35, 120.03, 118.70, 113.29, 98.74, 87.53, 66.14, 54.61; HRMS (ESI-TOF) calcd for $C_{20}H_{16}ClN_2O_2$ $[M+H]^+$ 351.0895, found 351.0894.

(*Z*)-5-(4-Chlorophenyl)-*N*-(2-(4,5-dihydrooxazol-2-yl)-phenyl)pent-2-en-4-ynamide (**3i**): 11.9 mg, 30% yield. White solid, m.p. 103～105 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.55 (s, 1H), 8.88 (d, J=8.4 Hz, 1H), 7.87 (dd, J=7.9, 1.5 Hz, 1H), 7.49 (t, J=8.0 Hz, 1H), 7.45 (d, J=8.4 Hz, 2H), 7.34 (d, J=8.4 Hz, 2H), 7.10 (t, J=7.6 Hz, 1H), 6.34 (d, J=11.5 Hz, 1H), 6.26 (d, J=11.5 Hz, 1H), 4.30 (t, J=9.5 Hz, 2H), 4.05 (t, J=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.55, 163.05, 139.67, 133.59, 133.37, 132.55, 131.59, 129.18, 123.33, 122.61, 121.86, 120.09, 118.66, 113.34, 98.78, 87.69, 66.16, 54.64; HRMS (ESI-TOF) calcd for $C_{20}H_{16}BrN_2O_2$ $[M+H]^+$ 395.0390, found 395.0386.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-(4-(trifluoromethyl)phenyl)pent-2-en-4-ynamide (**3j**): 14.6 mg, 38% yield. White solid, m.p. 113～115 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.58 (s, 1H), 8.88 (d, J=8.4 Hz, 1H), 7.87 (d, J=7.8 Hz, 1H), 7.60 (d, J=8.4 Hz, 2H), 7.57 (d, J=8.4 Hz, 2H), 7.49 (t, J=7.9 Hz, 1H), 7.11 (t, J=7.6 Hz, 1H), 6.38 (d, J=11.4 Hz, 1H), 6.29 (d, J=11.4 Hz, 1H), 4.31 (t, J=9.5 Hz, 2H), 4.06 (t, J=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.61, 162.85, 139.63, 134.34, 132.58, 132.16, 130.45 (q, J=32.6 Hz), 129.21, 126.70, 125.19 (q, J=3.8 Hz), 123.84 (q, J=272.5 Hz), 122.69, 120.07, 118.44, 113.34, 98.08, 88.66, 66.17, 54.64; ^{19}F NMR (471 MHz, $CDCl_3$) δ: －82.86; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_3N_2O_2$ $[M+H]^+$ 385.1158, found 385.1152.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-5-(thiophen-3-yl)pent-2-en-4-ynamide (**3k**): 12.9 mg, 40% yield. White solid, m.p. 101～103 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.55 (s, 1H), 8.88 (dd, J=8.4, 1.2 Hz, 1H), 7.86 (dd, J=7.8, 1.7 Hz, 1H), 7.52 (dd, J=3.0, 1.1 Hz, 1H), 7.48 (ddd, J=8.7, 7.4, 1.7 Hz, 1H), 7.27～7.24 (m, 1H), 7.13 (dd, J=5.0, 1.1 Hz, 1H), 7.10 (td, J=7.6, 1.1 Hz, 1H), 6.30 (d, J=11.5 Hz, 1H), 6.26 (d, J=11.5 Hz, 1H), 4.28 (t, J=9.5 Hz, 2H), 4.03 (t, J=9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.43, 163.25, 139.70, 132.92, 132.49, 130.08, 129.90, 129.14 , 125.34, 122.52, 122.04, 120.10, 118.79, 113.34, 95.30, 86.33, 66.16, 54.65; HRMS (ESI-TOF) calcd for $C_{18}H_{15}N_2O_2S$ $[M+H]^+$ 323.0849, found 323.0851.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)dec-2-en-4-ynamide (**3l**): 13.0 mg, 42% yield. White solid, m.p. 45～46 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.36 (s, 1H), 8.84 (dd, J=8.4, 1.1 Hz, 1H), 7.85 (dd, J=7.9, 1.6 Hz, 1H), 7.45 (ddd, J=8.6, 7.3, 1.6 Hz, 1H), 7.07 (td, J=7.6, 1.2 Hz, 1H), 6.19 (d, J=11.4 Hz, 1H), 6.08 (dt, J=11.4, 2.5 Hz, 1H), 4.37 (t, J=9.5 Hz, 2H), 4.13 (t, J=9.5 Hz, 2H), 2.42 (td, J=7.2, 2.4 Hz, 2H), 1.58～1.53 (m, 2H), 1.39～1.35 (m, 3H), 1.32～1.24 (m, 3H), 0.86 (t, J=7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.55, 163.31, 139.79, 132.43,

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132.01, 129.09, 122.36, 120.35, 120.15, 113.30, 102.98, 77.78, 66.13, 54.73, 31.12, 28.16, 22.18, 20.14, 13.87; HRMS (ESI-TOF) calcd for $C_{19}H_{23}N_2O_2$ $[M+H]^+$ 311.1754, found 311.1755.

(*Z*)-5-Cyclohexyl-*N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-pent-2-en-4-ynamide (**3m**): 17.0 mg, 53% yield. White solid, m.p. 85～87 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.32 (s, 1H), 8.83 (dd, J=8.5, 1.1 Hz, 1H), 7.84 (dd, J=7.9, 1.6 Hz, 1H), 7.45 (ddd, J=8.7, 7.4, 1.7 Hz, 1H), 7.07 (td, J=7.7, 1.2 Hz, 1H), 6.18 (d, J=11.5 Hz, 1H), 6.09 (dd, J=11.5, 2.3 Hz, 1H), 4.36 (t, J=9.5 Hz, 2H), 4.12 (t, J=9.5 Hz, 2H), 2.60 (tq, J=9.1, 3.2 Hz, 1H), 1.87～1.79 (m, 2H), 1.74～1.67 (m, 2H), 1.54～1.43 (m, 3H), 1.33～1.25 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.52, 163.37, 139.78, 132.41, 132.02, 129.07, 122.31, 120.23, 120.14, 113.27, 106.50, 77.70, 66.12, 54.73, 32.25, 30.26, 25.82, 24.82; HRMS (ESI-TOF) calcd for $C_{20}H_{23}FN_2O_2$ $[M+H]^+$ 323.1754, found 323.1755.

(*Z*)-5-Cyclopropyl-*N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)pent-2-en-4-ynamide (**3n**): 14.0 mg, 50% yield. White solid, m.p. 85～87 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.34 (s, 1H), 8.85 (dd, J=8.5, 1.1 Hz, 1H), 7.85 (dd, J=8.0, 1.6 Hz, 1H), 7.46 (ddd, J=8.7, 7.4, 1.7 Hz, 1H), 7.07 (td, J=7.6, 1.1 Hz, 1H), 6.16 (d, J=11.4 Hz, 1H), 6.03 (dd, J=11.4, 2.5 Hz, 1H), 4.37 (t, J=9.5 Hz, 2H), 4.13 (t, J=9.5 Hz, 2H), 1.49 (ttd, J=7.8, 5.0, 2.4 Hz, 1H), 0.87 (ddt, J=8.2, 5.8, 3.0 Hz, 2H), 0.81 (tt, J=5.1, 2.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.53, 163.29, 139.80, 132.44, 131.78, 129.09, 122.33, 120.37, 120.11, 113.25, 106.48, 73.58, 66.15, 54.71, 9.25, 0.99; HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$ 281.1285, found 281.1286.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-2-methyl-5-(*p*-tolyl)pent-2-en-4-ynamide (**3o**): 19.9 mg, 58% yield. White solid, m.p. 102～104 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.71 (s, 1H), 8.90 (dd, J=8.4, 1.1 Hz, 1H), 7.85 (dd, J=7.9, 1.6 Hz, 1H), 7.49 (ddd, J=8.7, 7.4, 1.7 Hz, 1H), 7.11 (t, J=7.5 Hz, 3H), 7.03 (d, J=7.9 Hz, 2H), 6.03 (d, J=1.7 Hz, 1H), 4.06 (t, J=9.8 Hz, 2H), 3.90 (t, J=9.8 Hz, 2H), 2.30 (s, 3H), 2.17 (d, J=1.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.57, 163.95, 144.01, 139.47, 138.59, 132.42, 131.31, 129.11, 128.97, 122.50, 120.17, 120.05, 113.76, 111.74, 95.98, 85.80, 66.04, 54.60, 21.43, 20.63; HRMS (ESI-TOF) calcd for $C_{22}H_{21}N_2O_2$ $[M+H]^+$ 345.1598, found 345.1598.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-2-phenyl-5-(*p*-tolyl)pent-2-en-4-ynamide (**3p**): 20.6 mg, 51% yield. White solid, m.p. 165～168 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.78 (s, 1H), 8.98 (d, J=8.4 Hz, 1H), 7.85 (dd, J=7.9, 1.7 Hz, 1H), 7.59～7.50 (m, 3H), 7.41～7.33 (m, 3H), 7.16～7.11 (m, 3H), 7.04 (d, J=7.8 Hz, 2H), 6.41 (s, 1H), 4.10 (t, J=9.5 Hz, 2H), 3.82 (t, J=9.5 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.39, 163.88, 147.70, 139.47, 138.78, 136.32, 132.46, 131.50, 129.02, 129.00, 128.75, 128.58, 127.13, 122.71, 120.19, 119.94, 113.80, 110.42, 98.18, 86.27, 66.05, 54.48, 21.48; HRMS (ESI-TOF) calcd for $C_{27}H_{23}N_2O_2$ $[M+H]^+$ 407.1754, found 407.1759.

(*Z*)-2-Benzyl-*N*-(2-(4,5-dihydrooxazol-2-yl)phenyl)-5-(*p*-tolyl)pent-2-en-4-ynamide (**3q**): 23.2 mg, 55% yield. White solid, m.p. 106～108 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.79 (s, 1H), 8.88 (d, J=8.5 Hz, 1H), 7.84 (dd, J=7.9, 1.6 Hz, 1H), 7.51～7.46 (m, 1H), 7.34～7.27 (m, 4H), 7.25～7.21 (m, 1H), 7.11 (t, J=7.7 Hz, 1H), 7.07 (d, J=8.0 Hz, 2H), 7.01 (d, J=7.9 Hz, 2H), 5.85 (s, 1H), 4.03 (t, J=9.4 Hz, 2H), 3.87 (t, J=9.4 Hz, 2H), 3.86 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.24, 163.81, 147.84, 139.40, 138.69, 138.00, 132.37, 131.30, 129.31, 129.06, 128.98, 128.55, 126.55, 122.54, 120.22, 119.96, 113.80, 112.16, 97.05, 85.57, 66.01, 54.62, 39.84, 21.42; HRMS (ESI-TOF) calcd for $C_{28}H_{25}N_2O_2$ $[M+H]^+$ 421.1911, found 421.1917.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-3-methyl-5-(*p*-tolyl)pent-2-en-4-ynamide (**3r**): 11.0 mg, 32% yield. White solid, m.p. 110～113 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.36 (s, 1H), 8.89 (d, J=8.5 Hz, 1H), 7.85 (dd, J=7.9, 1.6 Hz, 1H), 7.47 (ddd, J=8.7, 7.4, 1.6 Hz, 1H), 7.37 (d, J=7.9 Hz, 2H), 7.11 (d, J=7.9 Hz, 2H), 7.07 (t, J=7.6 Hz, 1H), 6.15 (d, J=1.5 Hz, 1H), 4.24 (t, J=9.5 Hz, 2H), 4.04 (t, J=9.5 Hz, 2H), 2.34 (s, 3H), 2.17 (d, J=1.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.46, 163.79, 140.04, 139.05, 132.45, 131.92, 130.24, 129.10, 129.01, 128.98, 122.16, 120.12, 119.92, 113.24, 99.68, 88.16, 66.08, 54.73, 25.24, 21.54; HRMS (ESI-TOF) calcd for $C_{22}H_{21}N_2O_2$ $[M+H]^+$ 345.1598, found 345.1595.

(*Z*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-3-phenyl-5-(*p*-tolyl)pent-2-en-4-ynamide (**3s**): 17.0 mg, 42% yield. Yellow solid, m.p. 172～175 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.63 (s, 1H), 8.96 (d, J=8.4 Hz, 1H), 7.87 (dd, J=7.9, 1.7 Hz, 1H), 7.83 (d, J=6.4 Hz, 2H), 7.51 (t, J=7.5 Hz, 1H), 7.44 (dt, J=9.0, 4.5 Hz, 5H), 7.14 (d, J=7.9 Hz, 2H), 7.10 (t, J=7.8 Hz, 1H), 6.70 (s, 1H), 4.24 (t, J=9.5 Hz, 2H), 4.03 (t, J=9.4 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.45, 163.91, 139.98, 139.31, 137.85, 132.49, 131.94, 129.39, 129.14, 129.08, 128.80, 128.58, 127.78, 127.15, 122.35, 120.19, 119.82, 113.34, 101.53, 86.66, 66.11, 54.73, 21.57; HRMS (ESI-TOF) calcd for $C_{27}H_{23}N_2O_2$ $[M+H]^+$ 407.1754, found 407.1754.

(*Z*)-3-(4-Chlorophenyl)-*N*-(2-(4,5-dihydrooxazol-2-yl)-phenyl)-5-(*p*-tolyl)pent-2-en-4-ynamide (**3t**): 17.1 mg, 39% yield. Yellow solid, m.p. 142～145 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.64 (s, 1H), 8.95 (dd, J=8.5, 1.1 Hz, 1H), 7.87 (dd, J=7.9, 1.6 Hz, 1H), 7.75 (d, J=8.6 Hz, 2H), 7.50 (ddd, J=8.7, 7.3, 1.7 Hz, 1H), 7.42 (dd, J=12.8, 8.3 Hz, 4H), 7.14 (d, J=7.9 Hz, 2H), 7.10 (td, J=7.7, 1.1 Hz, 1H), 6.66 (s, 1H), 4.24 (t, J=9.5 Hz, 2H), 4.03 (t, J=9.5 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.44, 163.57, 139.86, 139.49, 136.22, 135.38, 132.48, 131.91, 131.28, 129.14, 129.10, 128.73, 128.39, 127.80, 122.42, 120.11, 119.54, 113.29, 101.82, 86.25, 66.09, 54.68, 21.57; HRMS (ESI-TOF) calcd for $C_{27}H_{22}ClN_2O_2$ $[M+H]^+$ 441.1364, found 441.1362.

(*Z*)-3-(3-Bromophenyl)-*N*-(2-(4,5-dihydrooxazol-2-yl)-phenyl)-5-(*p*-tolyl)pent-2-en-4-ynamide (**3u**): 20.4 mg, 42% yield. Yellow solid, m.p. 147～150 ℃; ^{1}H NMR (500

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MHz, $CDCl_3$) δ: 12.66 (s, 1H), 8.95 (dd, J=8.6, 1.2 Hz, 1H), 7.95 (t, J=1.9 Hz, 1H), 7.87 (dd, J=7.9, 1.7 Hz, 1H), 7.74 (dd, J=7.9, 0.8 Hz, 1H), 7.54 (ddd, J=8.0, 1.9, 0.9 Hz, 1H), 7.51 (ddd, J=8.7, 7.4, 1.6 Hz, 1H), 7.44 (d, J=8.1 Hz, 2H), 7.31 (t, J=7.9 Hz, 1H), 7.14 (d, J=7.9 Hz, 2H), 7.11 (td, J=7.6, 1.2 Hz, 1H), 6.66 (s, 1H), 4.25 (t, J=9.5 Hz, 2H), 4.04 (t, J=9.5 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.41, 163.44, 139.88, 139.80, 139.53, 132.47, 132.23, 131.94, 130.99, 130.15, 130.04, 129.14, 129.10, 128.47, 125.69, 122.69, 122.47, 120.13, 119.48, 113.33, 101.92, 86.12, 66.10, 54.69, 21.57; HRMS (ESI-TOF) calcd for $C_{27}H_{22}BrN_2O_2$ $[M+H]^+$ 485.0859, found 485.0863.

(*E*)-*N*-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-3-(thiophen-2-yl)-5-(*p*-tolyl)pent-2-en-4-ynamide (**3v**): 19.0 mg, 46% yield. Yellow solid, m.p. 161～164 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.57 (s, 1H), 8.93 (dd, J=8.5, 1.1 Hz, 1H), 7.87 (dd, J=7.8, 1.6 Hz, 1H), 7.60 (dd, J=3.7, 1.2 Hz, 1H), 7.53～7.45 (m, 3H), 7.37 (dd, J=5.1, 1.2 Hz, 1H), 7.15 (d, J=7.9 Hz, 2H), 7.13～7.06 (m, 2H), 6.65 (s, 1H), 4.27 (t, J=9.5 Hz, 2H), 4.06 (t, J=9.5 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.44, 163.50, 142.56, 139.97, 139.49, 132.45, 131.95, 129.12, 129.09, 127.88, 127.79, 127.38, 126.18, 124.40, 122.30, 120.13, 119.50, 113.24, 100.24, 85.70, 66.11, 54.69, 21.59; HRMS (ESI-TOF) calcd for $C_{25}H_{21}N_2O_2S$ $[M+H]^+$ 413.1318, found 413.1328.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-2-((4-methoxyphenyl)ethynyl)cyclopent-1-ene-1-carboxamide (**3w**): 20.5 mg, 53% yield. White solid, m.p. 154～157 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.42 (s, 1H), 8.89 (dd, J=8.5, 1.2 Hz, 1H), 7.85 (dd, J=7.9, 1.7 Hz, 1H), 7.48 (ddd, J=8.7, 7.3, 1.7 Hz, 1H), 7.34 (d, J=2.1 Hz, 1H), 7.33 (d, J=2.1 Hz, 1H), 7.09 (td, J=7.6, 1.2 Hz, 1H), 6.82 (d, J=2.1 Hz, 1H), 6.80 (d, J=2.1 Hz, 1H), 4.16 (t, J=9.4 Hz, 2H), 3.92 (t, J=9.4 Hz, 2H), 2.90 (tt, J=7.6, 2.4 Hz, 2H), 2.78 (tt, J=7.9, 2.4 Hz, 2H), 2.02 (quint, J=7.7 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.14, 163.96, 159.92, 142.19, 139.88, 133.30, 132.39, 129.76, 129.14, 122.23, 120.41, 115.25, 113.90, 113.55, 98.97, 84.90, 66.11, 55.29, 54.66, 39.26, 33.81, 22.29; HRMS (ESI-TOF) calcd for $C_{24}H_{23}N_2O_3$ $[M+H]^+$ 387.1703, found 387.1704.

N-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-2-((4-methoxyphenyl)ethynyl)cyclohex-1-ene-1-carboxamide (**3x**): 19.2 mg, 48% yield. White sticky foam; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 12.50 (s, 1H), 8.91 (dd, J=8.5, 1.1 Hz, 1H), 7.83 (dd, J=7.9, 1.7 Hz, 1H), 7.48 (ddd, J=8.7, 7.3, 1.7 Hz, 1H), 7.12 (d, J=2.1 Hz, 1H), 7.11 (d, J=3.4 Hz, 1H), 7.10～7.07 (m, 1H), 6.73 (d, J=2.1 Hz, 1H), 6.72 (d, J=2.1 Hz, 1H), 4.06 (td, J=9.3, 1.3 Hz, 2H), 3.96～3.90 (td, J=9.3, 1.3 Hz, 2H), 3.77 (s, 3H), 2.53 (dq, J=6.1, 2.9 Hz, 2H), 2.42 (dq, J=5.9, 3.2 Hz, 2H), 1.73 (hept, J=6.1 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.28, 163.95, 159.53, 139.79, 139.75, 132.85, 132.40, 129.08, 122.21, 122.02, 120.16, 115.54, 113.80, 113.72, 94.78, 87.89, 66.01, 55.25, 54.71, 31.24, 26.70, 21.93, 21.80; HRMS (ESI-TOF) calcd for $C_{25}H_{25}N_2O_3$ $[M+H]^+$ 401.1860, found 401.1865.

Supporting Information Optimization Studies , typical Procedure for mmol-Scale reaction and ^{1}H NMR and ^{13}C NMR spectra for compounds **1** and **3**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

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