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PAPER

Efficient synthesis of *N*-(buta-2,3-dienyl) amides from terminal *N*-propargyl amides and their synthetic potential towards oxazoline derivatives†

Bo Chen,[a] Nan Wang,[b] Wu Fan[b] and Shengming Ma*[a,b]

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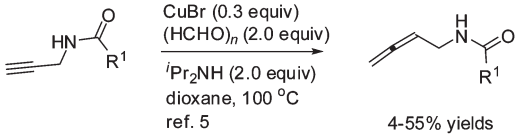
A series of *N*-allenyl amides was prepared conveniently from *N*-propargyl amides in good to excellent yields *via* a modified procedure developed in this group. The palladium-catalyzed coupling–cyclization of these prepared *N*-allenyl amides in the presence of organic iodides has been developed affording the oxazoline derivatives efficiently.

Introduction

In the past few decades, allene chemistry has experienced a veritable explosion.[1] Many natural products and pharmaceuticals with an allene moiety have also been identified.[2] Thus, methods for the synthesis of allenes from readily available starting materials are of high interest.[3] Among numerous methods developed, the reaction between terminal alkynes, aldehydes and amines is one of the most convenient methods for the synthesis of terminal or 1,3-disubstituted allenes.[4] In our recent report, many functional groups (such as hydroxyl group, ether, mesylate, alkylTsN-) may be introduced to terminal alkynes to prepare the corresponding terminal allenes.[4e] Recently, Hashmi synthesized the *N*-(buta-2,3-dienyl) amides under the i-Pr_2NH/CuBr conditions in very low yields (4–55%) (eqn (1)) for the synthesis of 1,3-oxazines.[5] We envisioned that the *N*-(buta-2,3-dienyl) amides may be prepared in much higher yields by utilizing the Cy_2NH/CuI protocol.[4e] Herein, we wish to report the efficient synthesis of these *N*-(buta-2,3-dienyl) amides and their application towards efficient synthesis of oxazolines[6–8] under the palladium catalysis.



(1)

[a]*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Linglin Lu, Shanghai 200032, P.R. China*
[b]*Shanghai Key Laboratory of Green Chemistry and Chemical Process, Department of Chemistry, East China Normal University, 3663 North Zhongshan Lu, Shanghai 200062, P.R. China.*
E-mail: masm@mail.sioc.ac.cn; Fax: (+86) 21-62609305

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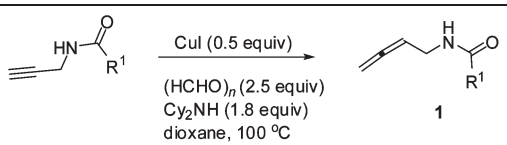
Results and discussion

In fact, by using the Cy_2NH/CuI protocol, the *N*-(buta-2,3-dienyl) amides **1** were efficiently synthesized from terminal *N*-propargyl amides in good to excellent yields with a wide substrate scope (Table 1). Different R^1 groups such as aryl, alkyl, benzyl groups may be tolerated (entries 1, 9 and 10). Electron-withdrawing (CO_2Et, halides) or electron-donating groups (Me, MeO) may be introduced to the aromatic ring (entries 2–7): aryl-containing substrates with electron-withdrawing groups afforded the products **1b–e** in higher yields (80–90%). A heteroaryl substituent such as 2-furanyl-substituted *N*-propargyl amide also worked well under the current reaction conditions, thus affording the *N*-(buta-2,3-dienyl) amide **1j** in 82% yield (entry 10). In

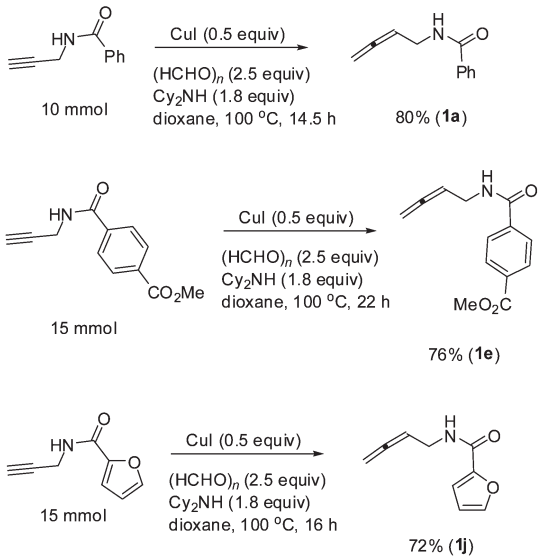
Table 1 Synthesis of the *N*-(buta-2,3-dienyl) amides **1**[a]



Entries	R^1	*t* (h)	Yield[b] (%)	Reported in ref. 5
1	Ph–	9	85 (**1a**)	34
2	*p*-FC_6H_4–	11.5	90 (**1b**)	
3	*p*-ClC_6H_4–	4.5	80 (**1c**)	
4	*p*-BrC_6H_4–	5.5	90 (**1d**)	
5	*p*-$MeO_2CC_6H_4$–	24	81 (**1e**)	
6	*p*-MeC_6H_4–	6	66 (**1f**)	
7	*p*-$MeOC_6H_4$–	1.2	76 (**1g**)	
8	*n*-C_4H_9–	2.7	73 (**1h**)	
9	Bn–	2.7	65 (**1i**)	
10	2-Furyl–	9.7	82 (**1j**)	55

[a] The reaction was carried out using 1 mmol of *N*-propargyl amide, 0.5 mmol of CuI, 2.5 mmol of $(HCHO)_n$, 1.8 mmol Cy_2NH in dioxane (2 mL) at 100 °C in a Schlenk tube. [b] Yields of the isolated products.

addition, three examples of 10 or 15 mmol scale syntheses also have been demonstrated (Scheme 1).

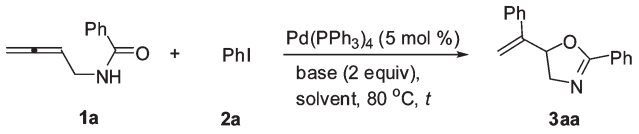


Scheme 1 The gram-scale preparation of **1**.

Recently, allenes have been used to synthesize various heterocycles efficiently.[1] To the best of our knowledge, very limited reports used an *N*-(buta-2,3-dienyl) amide motif in transition-metal-catalyzed reactions: Brummond *et al.*[9a] reported the cyclization of *N*-(buta-2,3-dienyl) amides affording 1,3-oxazines catalyzed by $AgNO_3$ or $AgBF_4$; Hashmi *et al.*[5] also realized the synthesis of 1,3-oxazines under the catalysis of $Au(PPh_3)Cl$/AgOTs/TsOH; Cook[9b] reported the palladium-catalyzed cyclization of *N*-(buta-2,3-dienyl) amides and aryl iodides affording oxazoline derivatives using our early reported conditions ($Pd(PPh_3)_4/K_2CO_3$/TBAB) for the intramolecular coupling–cyclization reaction of organic iodides with 2-(2′,3′-dienyl) malonates,[10] in which the *N*-(buta-2,3-dienyl) amides were prepared from amino acid derivatives in three steps (26–44% yields overall). In continuation of our work in this area,[11] we treated *N*-(buta-2,3-dienyl) amides **1a** with iodobenzene **2a** catalyzed by [$Pd(PPh_3)_4$] (5 mol%) in DMF at 80 °C with different bases. The reaction is complicated with KO^{t}Bu as the base (Table 1, entry 1). Then we switched to weaker bases and found the desired product **3aa** was formed exclusively in 90% NMR yield in the presence of K_2CO_3! Na_2CO_3, Cs_2CO_3 or Li_2CO_3 gave slightly lower yields with longer reaction times (Table 1, entries 2–5). After screening of the solvent effect, we found the reaction proceeded smoothly in almost all the solvents tested affording **3aa** in good yields. The reaction proceeds faster in the polar solvent and DMF gave the best result (Table 2, entries 6–11). Thus, we defined the reaction of **1a** (1 equiv.) and **2a** (1.2 equiv.) catalyzed by [$Pd(PPh_3)_4$] (5 mol%) with K_2CO_3 (2 equiv.) as the base in DMF at 80 °C as the standard conditions for further study.

With the optimized protocol in hand, we turned to demonstrate the generality of this reaction. As listed in Table 3, a variety of oxazoline derivatives could be prepared by the reaction between *N*-(buta-2,3-dienyl) amides and organic iodides. The aryl iodides

Table 2 Optimization of the reaction conditions[a]

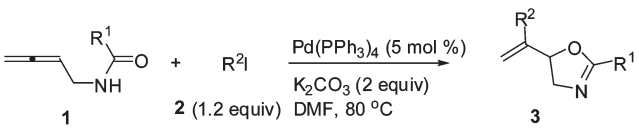


1a **2a** **3aa**

Entries	Solvent	*t* (h)	Base	**3aa**[b] (%)
1	DMF	2	KO^{t}Bu	0
2	DMF	37	Li_2CO_3	34[c]
3	DMF	10.3	Na_2CO_3	74
4	**DMF**	**3**	**K_2CO_3**	**90**
5	DMF	10.3	Cs_2CO_3	87
6	DMSO	5.3	K_2CO_3	82
7	DCE	19	K_2CO_3	23[d]
8	DMA	7.5	K_2CO_3	89
9	CH_3CN	24	K_2CO_3	88
10	Toluene	46	K_2CO_3	85
11	Dioxane	46	K_2CO_3	84

[a] The reaction was carried out using 0.2 mmol of **1a**, 0.24 mmol of **2a**, $Pd(PPh_3)_4$ (5 mol%) and base (2 equiv.) in the indicated solvent (2 mL) in a Schlenk tube. [b] The yields were determined by NMR using mesitylene as an internal standard. [c] The substrate **1a** was recovered by 23% NMR yield. [d] The substrate **1a** was recovered by 62% NMR yield. DMSO = dimethyl sulfoxide, DMF = *N*,*N*-dimethylformamide, DMA = *N*,*N*-dimethyl acetamide, DCE = dichloroethane.

Table 3 Palladium-catalyzed coupling–cyclization of *N*-(buta-2,3-dienyl) amides and organic iodides[a]



1 **2** (1.2 equiv) **3**

Entry	R^1 (**1**)	R^2 (**2**)	Time (h)	**3**[b] (%)
1	Ph (**1a**)	Ph (**2a**)	3	80 (**3aa**)
2	Ph (**1a**)	4-$MeOC_6H_4$ (**2b**)	8	69 (**3ab**)
3	Ph (**1a**)	4-MeC_6H_4 (**2c**)	9	66 (**3ac**)
4	Ph (**1a**)	4-BrC_6H_4 (**2d**)	17.5	83 (**3ad**)
5	Ph (**1a**)	4-FC_6H_4 (**2e**)	10	82 (**3ae**)
6	Ph (**1a**)	4-ClC_6H_4 (**2f**)	17	71 (**3af**)
7	Ph (**1a**)	4-$EtO_2CC_6H_4$ (**2g**)	9	91 (**3ag**)
8	Ph (**1a**)	4-$CH_3COC_6H_4$ (**2h**)	45.5	63 (**3ah**)
9	Ph (**1a**)	4-$O_2NC_6H_4$ (**2i**)	24	82 (**3ai**)
10	Ph (**1a**)	4-NCC_6H_4 (**2j**)	22	88 (**3aj**)
11	Ph (**1a**)	4-PhC_6H_4 (**2k**)	5	77 (**3ak**)
12	Ph (**1a**)	3-MeC_6H_4 (**2l**)	6	79 (**3al**)
13	Ph (**1a**)	3-FC_6H_4 (**2m**)	10	94 (**3am**)
14	Ph (**1a**)	2-MeC_6H_4 (**2n**)	28	66 (**3an**)
15	Ph (**1a**)	3-Thienyl (**2o**)	9	79 (**3ao**)
16	Ph (**1a**)	*N*-Tosyl-3-indolyl (**2p**)	9.5	66 (**3ap**)
17	Ph (**1a**)	(*E*)-PhCH=CH (**2q**)	6.5	58 (**3aq**)
18	Ph (**1a**)	(*E*)-^{n}BuCH=CH (**2r**)	6.5	77 (**3ar**)
19	4-FC_6H_4 (**1b**)	Ph (**2a**)	21	73 (**3ba**)
20	4-ClC_6H_4 (**1c**)	Ph (**2a**)	5	72 (**3ca**)
21	4-BrC_6H_4 (**1d**)	Ph (**2a**)	10	89 (**3da**)
22	4-$MeO_2CC_6H_4$ (**1e**)	Ph (**2a**)	10	86 (**3ea**)
23	4-MeC_6H_4 (**1f**)	Ph (**2a**)	5	87 (**3fa**)
24	4-$MeOC_6H_4$ (**1g**)	Ph (**2a**)	9	76 (**3ga**)
25	^{n}Bu (**1h**)	Ph (**2a**)	8	53 (**3ha**)
26	Bn (**1i**)	Ph (**2a**)	6.4	52 (**3ia**)
27	2-Furanyl (**1j**)	Ph (**2a**)	22	71 (**3ja**)

[a] The reaction was carried out using 0.2 mmol of **1**, 0.24 mmol of **2**, $Pd(PPh_3)_4$ (5 mol%) and K_2CO_3 (2 equiv.) in DMF (2 mL) at 80 °C in a Schlenk tube. [b] Yields of the isolated products.

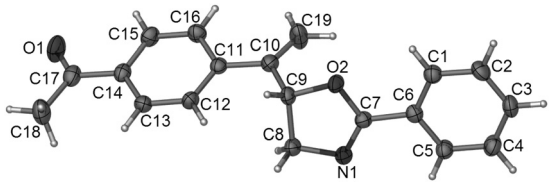
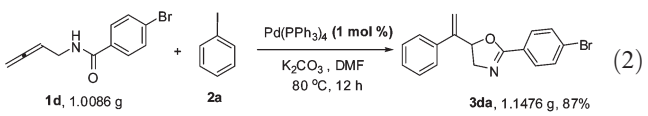
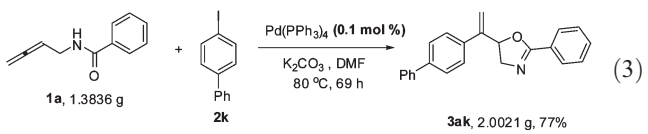


Fig. 1 ORTEP representation of **3ah**.

with electron-donating (MeO, Me) and electron-withdrawing (F, Cl, Br, Ph, CO_2Et, acetyl, NO_2, CN) substituents in the *para*-, *ortho*-, or *meta*-position of the aryl group are all suitable for this transformation, affording corresponding oxazoline derivatives in good to excellent yields (Table 3, entries 1–14). The reaction of heterocyclic aromatic iodides such as 3-iodo-1-tosyl-1*H*-indole or 3-iodothiophene also proceeded smoothly affording the corresponding products **3ao** or **3ap** in 66% and 79% yields, respectively (Table 3, entries 15 and 16). The reaction may also be extended to 1-alkenyl iodides (Table 3, entries 17 and 18). The structures of the products were unambiguously confirmed by the X-ray single crystal diffraction study of compound **3ah** (Fig. 1).[12] For R^1, various substituted aryl groups may be accommodated to afford the oxazoline derivatives in good to excellent yields (Table 3, entries 19–24); in addition, R^1 may also be 2-furanyl or even an alkyl or benzyl group (Table 3, entries 25–27). Furthermore, the reaction may be easily conducted in a scale of 1 g of the substrates catalyzed by 1 mol% or even 0.1 mol% $Pd(PPh_3)_4$ in 87% and 77% yields, respectively (eqn (2) and (3)).



(2)



(3)

Conclusion

In conclusion, we have presented a practical method for the synthesis of *N*-(buta-2,3-dienyl) amides by applying dicyclohexylamine/CuI and their synthetic potential towards oxazolines was also disclosed. This method for the synthesis of oxazoline derivatives has several advantages such as mild reaction conditions, good functional group tolerance, low-catalyst loading (up to 0.1 mol%), high yields, and easily accessible starting materials with diversity, thus it will stimulate studies on the synthesis of new oxazolines[6,7] with promising potential in industrial chemistry and asymmetric catalysis. Further studies on the development of an asymmetric version are being actively pursued in this laboratory.

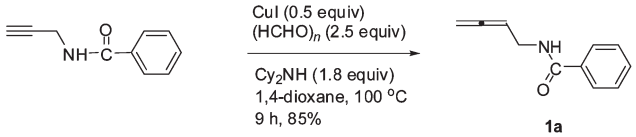
Experimental section

Materials

Starting materials *N*-propargyl amides were prepared according to known procedures.[13]

1. Experimental details for the results presented in Table 1

*(1) Synthesis of N-(buta-2,3-dienyl) benzamide (**1a**).*

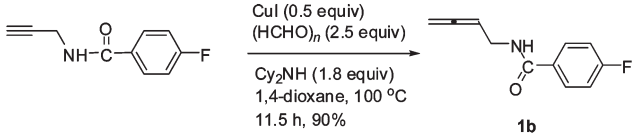


Typical procedure I: To an oven-dried reaction tube were added CuI (54.9 mg, 0.5 mmol), paraformaldehyde (75.9 mg, 2.5 mmol), *N*-propargyl benzamide (158.4 mg, 1 mmol), dioxane (2 mL), and dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol) sequentially under an argon atmosphere. The resulting mixture was then submerged in an oil bath preheated to 100 °C. When the reaction was complete as monitored by TLC, the mixture was cooled to rt, transferred with ether (50 mL) and filtrated through a short pad (3 cm) of silica gel. Evaporation and column chromatography on silica gel (petroleum ether–ethyl acetate = 5 : 1) afforded **1a**[5] (146.4 mg, 85%): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83–7.74 (m, 2H, ArH), 7.55–7.38 (m, 3H, ArH), 6.53 (bs, 1H, NH), 5.39–5.26 (m, 1H, C═CH), 4.90–4.84 (m, 2H, C═CH_2), 4.06–3.97 (m, 2H, NCH_2).

Gram-scale synthesis of **1a**: To a 100 mL three-necked flask equipped with a reflux condenser were added CuI (0.5491 g, 5 mmol), paraformaldehyde (0.7519 g, 25 mmol), dioxane (20 mL), *N*-propargyl benzamide (1.6097 g, 10 mmol), and dicyclohexylamine (3.6 mL, d = 0.916 g mL^{-1}, 3.264 g, 18 mmol) sequentially. The resulting mixture was then submerged in an oil bath preheated to 100 °C. After 14.5 h as monitored by TLC, the resulting mixture was then cooled to room temperature and concentrated under vacuum to a gummy residue. The residue was diluted with 100 mL of ether, washed sequentially with diluted (5%) hydrochloride acid (10 mL × 2), brine (10 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtrated and evaporated. Chromatography on silica gel (petroleum ether–ethyl acetate = 5 : 1) afforded **1a**[5] (1.3945 g, 80%): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81–7.75 (m, 2H, ArH), 7.55–7.38 (m, 3H, ArH), 6.33 (bs, 1H, NH), 5.40–5.26 (m, 1H, C═CH), 4.98–4.84 (m, 2H, C═CH_2), 4.10–4.00 (m, 2H, NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 167.4, 134.3, 131.3, 128.4, 126.9, 87.9, 77.6, 37.8; IR (neat) 3271, 1952, 1627, 1603, 1577, 1545, 1490, 1435, 1329, 1305, 1250, 1063, 1032 cm^{-1}; MS (EI) m/z (%) 173 (M^+, 18.85), 105 (100).

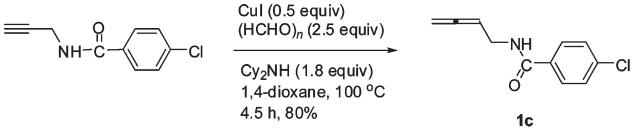
The following compounds were prepared according to typical procedure I.

*(2) Synthesis of N-(buta-2,3-dienyl) 4-fluorobenzamide (**1b**).*



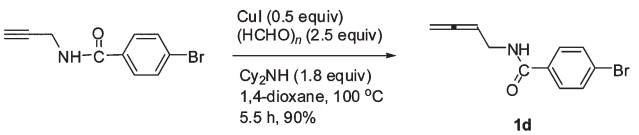
The reaction of CuI (54.9 mg, 0.5 mmol), paraformaldehyde (75.1 mg, 2.5 mmol), *N*-propargyl 4-fluorobenzamide (177.3 mg, 1 mmol), dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol), and dioxane (2 mL) afforded **1b** (171.6 mg, 90%) (eluent : petroleum ether–ethyl acetate = 5 : 1): solid; mp 88–89 °C (petroleum ether–ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85–7.72 (m, 2H, ArH), 7.10 (t, J = 8.3 Hz, 2H, ArH), 6.46 (bs, 1H, NH), 5.39–5.28 (m, 1H, C═CH), 4.90–4.86 (m, 2H, C═CH_2), 4.08–3.98 (m, 2H, NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 166.3, 164.6 (d, J = 249.8 Hz), 130.5 (d, J = 3.2 Hz), 129.2 (d, J = 9.2 Hz), 115.5 (d, J = 21.1 Hz), 87.9, 77.8, 37.9; ^{19}F NMR ($CDCl_3$, 282 MHz) −108.3; IR (neat) 3278, 1954, 1631, 1603, 1547, 1501, 1424, 1356, 1328, 1289, 1232, 1161, 1111, 1061, 1013 cm^{-1}; MS (EI) m/z (%) 191 (M^+, 18.20), 123 (100); anal. calcd for $C_{11}H_{10}FNO_2$: C, 69.10; H, 5.27; N, 7.33; found: C, 69.03; H, 5.28; N, 7.32.

*(3) Synthesis of N-(buta-2,3-dienyl) 4-chlorobenzamide (**1c**).*



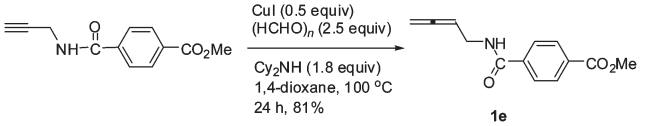
The reaction of CuI (54.8 mg, 0.5 mmol), paraformaldehyde (74.7 mg, 2.5 mmol), *N*-propargyl 4-chlorobenzamide (193.3 mg, 1 mmol), dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol), and dioxane (2 mL) afforded **1c** (165.0 mg, 80%) (eluent : petroleum ether–ethyl acetate = 5 : 1): solid; mp 85–86 °C (*n*-hexane–ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, J = 7.8 Hz, 2H, ArH), 7.34 (d, J = 7.8 Hz, 2H, ArH), 7.21 (bs, 1H, NH), 5.35–5.22 (m, 1H, C═CH), 4.86–4.76 (m, 2H, C═CH_2), 4.08–3.90 (m, 2H, NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.0, 166.2, 137.7, 132.8, 128.8, 128.3, 87.9, 78.0, 37.9; IR (neat) 3281, 1953, 1630, 1596, 1543, 1486, 1422, 1325, 1292, 1277, 1244, 1183, 1148, 1114, 1092, 1061, 1013 cm^{-1}; MS (EI) m/z (%) 209 ($M(^{37}Cl)^+$, 8.97), 207 ($M(^{35}Cl)^+$, 24.01), 139 (100); anal. calcd for $C_{11}H_{10}ClNO$: C, 63.62; H, 4.85; N, 6.75; found: C, 63.52; H, 4.93; N, 6.80.

*(4) Synthesis of N-(buta-2,3-dienyl) 4-bromobenzamide (**1d**).*



The reaction of CuI (54.7 mg, 0.5 mmol), paraformaldehyde (75.4 mg, 2.5 mmol), *N*-propargyl 4-bromobenzamide (237.8 mg, 1 mmol), dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol), and dioxane (2 mL) afforded **1d** (225.9 mg, 90%) (eluent : petroleum ether–ethyl acetate = 5 : 1): solid; mp 90–91 °C (*n*-hexane–ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 8.4 Hz, 2H, ArH), 7.57 (d, J = 8.4 Hz, 2H, ArH), 6.34 (bs, 1H, NH), 5.41–5.28 (m, 1H, C═CH), 4.95–4.84 (m, 2H, C═CH_2), 4.09–3.95 (m, 2H, NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 166.3, 133.2, 131.8, 128.5, 126.2, 87.8, 78.0, 37.9; IR (neat) 3287, 2926, 1957, 1631, 1591, 1542, 1483, 1423, 1357, 1331, 1292, 1245, 1190, 1145, 1113, 1073, 1062, 1011 cm^{-1}; MS (EI) m/z (%) 253 ($M(^{81}Br)^+$, 20.70), 251 ($M(^{79}Br)^+$, 26.75), 183 (100); anal. calcd for $C_{11}H_{10}BrNO$: C, 52.41; H, 4.00; N, 5.56; found: C, 52.42; H, 4.16; N, 5.47.

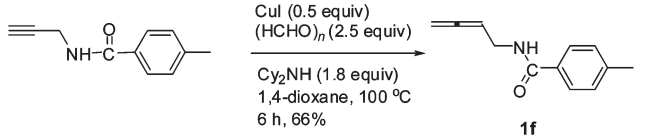
*(5) Synthesis of N-(buta-2,3-dienyl) 4-carbomethoxy benzamide (**1e**).*



The reaction of CuI (54.4 mg, 0.5 mmol), paraformaldehyde (75.3 mg, 2.5 mmol), *N*-propargyl 4-carbomethoxy benzamide (217.2 mg, 1 mmol), dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol), and dioxane (2 mL) afforded **1e** (187.3 mg, 81%) (eluent : petroleum ether–ethyl acetate = 3 : 1): solid; mp 126–127 °C (*n*-hexane–ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 2H, ArH), 7.84 (d, J = 8.4 Hz, 2H, ArH), 6.36 (bs, 1H, NH), 5.40–5.26 (m, 1H, C═CH), 4.99–4.85 (m, 2H, C═CH_2), 4.15–4.02 (m, 2H, NCH_2), 3.95 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.0, 166.5, 166.2, 138.2, 132.4, 129.5, 126.9, 87.7, 77.5, 52.2, 38.0; IR (neat) 3296, 2925, 2852, 1956, 1727, 1633, 1549, 1504, 1437, 1357, 1335, 1283, 1243, 1195, 1149, 1112, 1062, 1020 cm^{-1}; MS (EI) m/z (%) 231 (M^+, 38.15), 230 ($M^+ - 1$, 3.52), 163 (100); anal. calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06; found: C, 67.49; H, 5.55; N, 6.12.

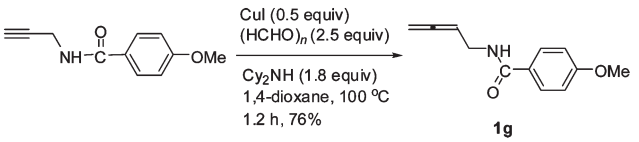
Gram scale synthesis of **1e**: The reaction of CuI (0.830 g, 7.6 mmol), paraformaldehyde (1.126 g, 37.5 mmol), *N*-propargyl 4-carbomethoxy benzamide (3.166 g, 14.6 mmol), dicyclohexylamine (5.3 mL, d = 0.916 g mL^{-1}, 4.9 g, 27 mmol) and dioxane (40 mL) in 22 h afforded **1e** (2.5644 g, 76%) (eluent: petroleum ether–ethyl acetate = 10 : 1 to 1 : 1): solid; mp 126–127 °C (*n*-hexane–ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 2H, ArH), 7.85 (d, J = 8.7 Hz, 2H, ArH), 7.10 (bs, 1H, NH), 5.36–5.25 (m, 1H, C═CH), 4.88–4.81 (m, 2H, C═CH_2), 4.08–4.00 (m, 2H, NCH_2), 3.93 (s, 3H, OCH_3).

*(6) Synthesis of N-(buta-2,3-dienyl) 4-methyl benzamide (**1f**).*



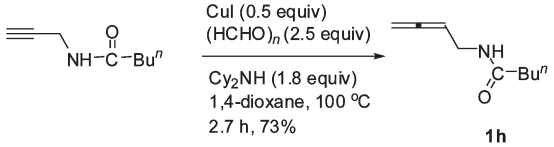
The reaction of CuI (55.1 mg, 0.5 mmol), paraformaldehyde (75.6 mg, 2.5 mmol), *N*-propargyl 4-methyl benzamide (173.8 mg, 1 mmol), dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol), and dioxane (2 mL) afforded **1f** (124.3 mg, 66%) (eluent: petroleum ether–ethyl acetate = 5 : 1): solid; mp 67–68 °C (*n*-hexane–ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 8.1 Hz, 2H, ArH), 7.20 (d, J = 8.1 Hz, 2H, ArH), 6.63 (bs, 1H, NH), 5.37–5.25 (m, 1H, C═CH), 4.90–4.82 (m, 2H, C═CH_2), 4.09–3.95 (m, 2H, NCH_2), 2.38 (s, 3H, $ArCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.0, 167.2, 141.8, 131.6, 129.2, 126.9, 88.1, 77.7, 37.8, 21.4; IR (neat) 3285, 2917, 1955, 1624, 1545, 1507, 1424, 1352, 1287, 1241, 1193, 1149, 1123, 1061, 1021 cm^{-1}; MS (EI) m/z (%) 187 (M^+, 31.03), 119 (100); anal. calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48; found: C, 76.88; H, 6.94; N, 7.42.

*(7) Synthesis of N-(buta-2,3-dienyl) 4-methoxyl benzamide (**1g**).*



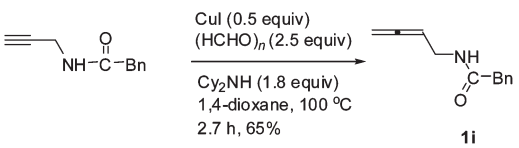
The reaction of CuI (54.8 mg, 0.5 mmol), paraformaldehyde (75.3 mg, 2.5 mmol), *N*-propargyl 4-methoxyl benzamide (188.7 mg, 1 mmol), dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol), and dioxane (2 mL) afforded **1g** (153.3 mg, 76%) (eluent: petroleum ether–ethyl acetate = 3 : 1): solid; mp 90–92 °C (*n*-hexane–ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H, ArH), 6.92 (d, J = 8.4 Hz, 2H, ArH), 6.34 (bs, 1H, NH), 5.39–5.26 (m, 1H, C═CH), 4.93–4.82 (m, 2H, C═CH_2), 4.08–3.97 (m, 2H, NCH_2), 3.84 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 166.8, 162.1, 128.7, 126.7, 113.7, 88.1, 77.7, 55.3, 37.8; IR (neat) 3322, 2929, 2853, 1957, 1633, 1612, 1575, 1539, 1507, 1460, 1445, 1325, 1308, 1286, 1256, 1180, 1113, 1064, 1026 cm^{-1}; MS (EI) m/z (%) 203 (M^+, 27.34), 135 (100); anal. calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89; found: C, 71.17; H, 6.41; N, 6.85.

*(8) Synthesis of N-(buta-2,3-dienyl) pentanamide (**1h**).*



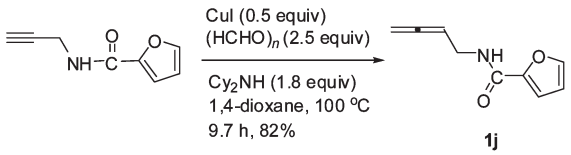
The reaction of CuI (54.6 mg, 0.5 mmol), paraformaldehyde (75.5 mg, 2.5 mmol), *N*-propargyl pentanamide (140.0 mg, 1 mmol), dioxane (2 mL), and dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol) afforded **1h** (111.7 mg, 73%) (petroleum ether–ethyl acetate = 5 : 1): oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (bs, 1H, NH), 5.28–5.18 (m, 1H, C═CH), 4.88–4.81 (m, 2H, C═CH_2), 3.89–3.81 (m, 2H, NCH_2), 2.20 (t, J = 7.7 Hz, 2H, $COCH_2$), 1.68–1.54 (m, 2H, CH_2), 1.42–1.26 (m, 2H, CH_2), 0.92 (t, J = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 173.0, 88.1, 77.6, 37.3, 36.4, 27.8, 22.4, 13.8; IR (neat) 3290, 3078, 2958, 2931, 2872, 1958, 1645, 1544, 1429, 1354, 1268, 1198, 1118, 1059 cm^{-1}; MS (EI) m/z (%) 153 (M^+, 71.49), 85 (100); HRMS calcd for $C_9H_{15}NO$ (M^+): 153.1154, found: 153.1156.

*(9) Synthesis of N-(buta-2,3-dienyl) 2-phenylacetamide (**1i**).*



The reaction of CuI (54.8 mg, 0.5 mmol), paraformaldehyde (74.9 mg, 2.5 mmol), *N*-propargyl 2-phenylacetamide (172.8 mg, 1 mmol), dioxane (2 mL), and dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol) afforded **1i** (121.7 mg, 65%) (petroleum ether–ethyl acetate = 5 : 1): oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.20 (m, 5H, ArH), 5.88 (bs, 1H, NH), 5.19–5.08 (m, 1H, C═CH), 4.77–4.68 (m, 2H, C═CH_2), 3.82–3.75 (m, 2H, NCH_2), 3.57 (s, 2H, CH_2Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4, 170.7, 134.6, 129.5, 128.9, 127.3, 87.8, 77.8, 43.6, 37.2; IR (neat) 3269, 3084, 2922, 1961, 1643, 1562, 1492, 1438, 1421, 1332, 1319, 1266, 1193, 1164, 1030 cm^{-1}; MS (EI) m/z (%) 187 (M^+, 25.95), 91 (100); HRMS calcd for $C_{12}H_{13}NO$ (M^+): 187.0997, found: 187.1000.

*(10) Synthesis of N-(buta-2,3-dienyl) furan-2-carboxamide (**1j**).*

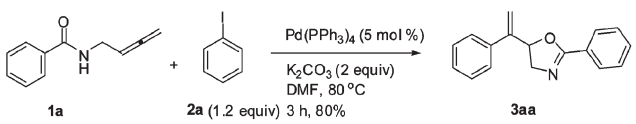


The reaction of CuI (54.4 mg, 0.5 mmol), paraformaldehyde (75.3 mg, 2.5 mmol), *N*-propargyl furan-2-carboxamide (150.0 mg, 1 mmol), dioxane (2 mL), and dicyclohexylamine (0.36 mL, d = 0.916 g mL^{-1}, 326.4 mg, 1.8 mmol) afforded **1j**[5] (133.8 mg, 82%) (petroleum ether–ethyl acetate = 3 : 1): oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (s, 1H, ArH), 7.13–7.08 (m, 1H, ArH), 6.64 (bs, 1H, NH), 6.49 (s, 1H, ArH), 5.38–5.22 (m, 1H, C═CH), 4.90–4.81 (m, 2H, C═CH_2), 4.07–3.95 (m, 2H, NCH_2).

Gram scale synthesis of **1j**: The reaction of CuI (0.8370 g, 7.5 mmol), paraformaldehyde (1.1340 g, 37.5 mmol), *N*-propargyl furan-2-carboxamide (2.2610 g, 15 mmol), dioxane (40 mL), and dicyclohexylamine (5.3 mL, d = 0.916 g mL^{-1}, 4.8548 g, 27 mmol) in 16 h afforded **1j**[5] (1.7809 g, 72%) (petroleum ether–ethyl acetate = 5 : 1): oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46–7.42 (m, 1H, ArH), 7.12 (d, J = 3.6 Hz, 1H, ArH), 6.57 (bs, 1H, NH), 6.52–6.46 (m, 1H, ArH), 5.41–5.23 (m, 1H, C═CH), 4.91–4.82 (m, 2H, C═CH_2), 4.07–3.96 (m, 2H, NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 158.1, 147.6, 143.8, 113.9, 111.8, 87.5, 77.3, 37.1; IR (neat) 3305, 1958, 1645, 1593, 1572, 1523, 1474, 1429, 1358, 1294, 1242, 1227, 1184, 1079, 1013 cm^{-1}; MS (EI) m/z (%) 163 (M^+, 100), 95 (100).

2. Experimental details for the results presented in entry 1, Table 3

*Synthesis of 2-phenyl-5-(1-phenylvinyl)-4,5-dihydrooxazole (**3aa**).*



Typical procedure II: After the Schlenk tube containing K_2CO_3 (55.4 mg, 0.4 mmol) was flame-dried and filled with nitrogen, $Pd(PPh_3)_4$ (11.7 mg, 0.01 mmol), **1a** (34.9 mg, 0.2 mmol), **2a** (49.7 mg, 0.24 mmol), and DMF (2 mL) were added sequentially. The resulting solution was stirred at 80 °C. When the reaction was completed as monitored by TLC, the mixture was diluted with diethyl ether (50 mL) and washed with water (5 mL × 3). Then the combined organic layer was dried over anhydrous Na_2SO_4, filtrated and evaporated. The residue was purified by chromatography on silica gel (eluent: petroleum ether–ethyl acetate = 10 : 1) to afford **3aa** (40.3 mg, 80%): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06–7.97 (m, 2H, ArH), 7.55–7.24

(m, 8H, ArH), 5.61 (t, J = 9.0 Hz, 1H, OCH), 5.46 (s, 1H, one proton in C=CH_2), 5.42 (s, 1H, one proton in C=CH_2), 4.29 (dd, J = 14.7, 10.2 Hz, 1H, one proton in NCH_2), 3.80 (dd, J = 14.7, 7.8 Hz, 1H, one proton in NCH_2) (for more detail about ^{1}H NMR, see ESI†); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 146.8, 137.9, 131.3, 128.5, 128.3, 128.1, 128.0, 127.6, 126.5, 112.4, 80.0, 61.0; IR (neat) 3059, 2927, 2870, 1652, 1579, 1495, 1448, 1335, 1257, 1177, 1082, 1062, 1025 cm^{-1}; MS (EI) m/z (%) 249 (M^+, 21.13), 117 (100); HRMS calcd for $C_{17}H_{15}NO$ [M^+]: 249.1154; found: 249.1152.

Acknowledgements

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12 Crystal data for **4ai**: $C_{19}H_{17}NO_2$, MW = 291.34, triclinic; space group $P\bar{1}$, final R indices [$I > 2\sigma(I)$], R_1 = 0.0374, wR_2 = 0.0934; a = 8.3211(5) Å, b = 9.7981(6) Å, c = 10.1922(6) Å, α = 73.183(2), β = 70.006(2)°, γ = 85.591(2)°, V = 747.28(8) A^3, T = 173(2) K, Z = 2, reflections collected/unique 8766/2612 [R(int) = 0.0222], number of observations [>2$\sigma(I)$] 2115, parameters: 207. CCDC 888586 contains the supplementary crystallographic data for this paper.

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