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TRANSITION METAL-FREE CYCLIZATION OF *N*-BOC-*N*-PROPARGYLENAMINES

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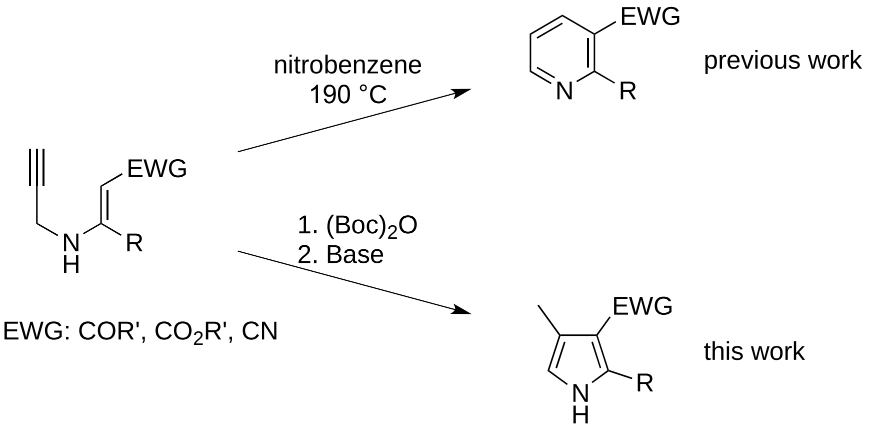
Abstract – An efficient method for the synthesis of multi-substituted pyrroles was developed using basic cyclization of readily accessible *N*-Boc-*N*-propargylenamines. Despite the basic conditions, cleavage of the *N*-Boc group occurred easily. The process was rapid and afforded *N*-H-pyrroles with wide functional group tolerance in high yields.

INTRODUCTION

Pyrrole skeletons are widely found in natural products[1] and functional materials,[2] and new methods for their synthesis are important in synthetic organic chemistry. Polysubstituted pyrroles are often used as synthetic intermediates for pharmaceuticals.[3] For example, atorvastatin, which reduces blood cholesterol, and sunitinib, which inhibits the growth of cancer cells. Therefore, development of a simple method for constructing a pyrrole skeleton is important. To date, a number of synthetic methods have been developed. Recently, many syntheses using intramolecular[4] and intermolecular[5] cyclizations with transition metal catalysts have been reported. However, the requisite transition metal catalysts are subject to stringent limitations for residues in pharmaceuticals set by the International Council for Harmonization.[6] For sustainable chemistry and environmental protection, transition metal-free conditions are valuable. Metal-free routes have been developed by several groups.[7] Recently, we developed a thermal annulation method for facile preparation of 2,3-disubstituted pyridines from easily accessible *N*-propargylenamines[8] (Scheme 1). Metal-free and additive-free synthesis of pyridine derivatives has been developed as an environmentally friendly technique. Annulation is tolerant of various enamine derivatives with electron withdrawing groups such as amides, ketones, esters, and nitriles. However, unstable enamines are not suitable and require a stabilization with a protecting group as *N*-Boc-enamines. Herein, we report a base-promoted annulation of *N*-Boc-*N*-propargylenamines. Unlike thermal annulation of *N*-propargylenamines, annulation of 5-*exo-dig* with various bases proceeded to afford pyrroles.



Scheme 1. Synthesis of transition metal-free pyridines and pyrroles via annulation of *N*-propargylenamines

RESULTS AND DISCUSSION

Initial attempts to synthesize the desired *N*-Boc-*N*-propargylenamine cyclization precursor focused on a one-pot preparation with condensation and protection (Scheme 2). For the condensation of ketones with propargylamine in this study, the reactions under solvent-free conditions occurred faster than in the presence of solvent, and the desired enamines are obtained in nearly pure forms after simple evaporation of volatile substances. On the other hand, ethanol was sometimes required for this type of condensation due to its high solubility to the starting materials employed. Moreover, acetic acid was applied, as the solvent, to the starting materials having nitrile groups. Protection of *N*-H of **2** with $(Boc)_2O$ was difficult because of the low nucleophilicity of nitrogen in the enamine analogs, but the desired *N*-Boc precursors were obtained in excellent yields using a catalytic amount of DMAP.

Most of the products (**3**) were confirmed to be a single isomer by ^{1}H NMR spectra. NOESY experiments showed that **3aa** and **3ay** were in the *E*-configuration by the correlation between propargyl and vinylic proton (Figure 1).

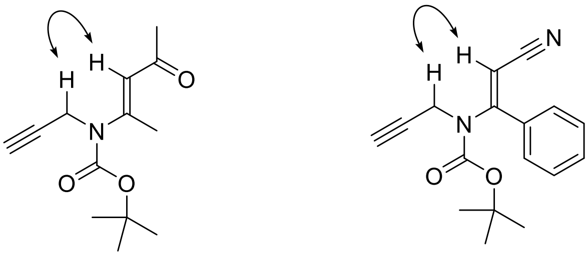
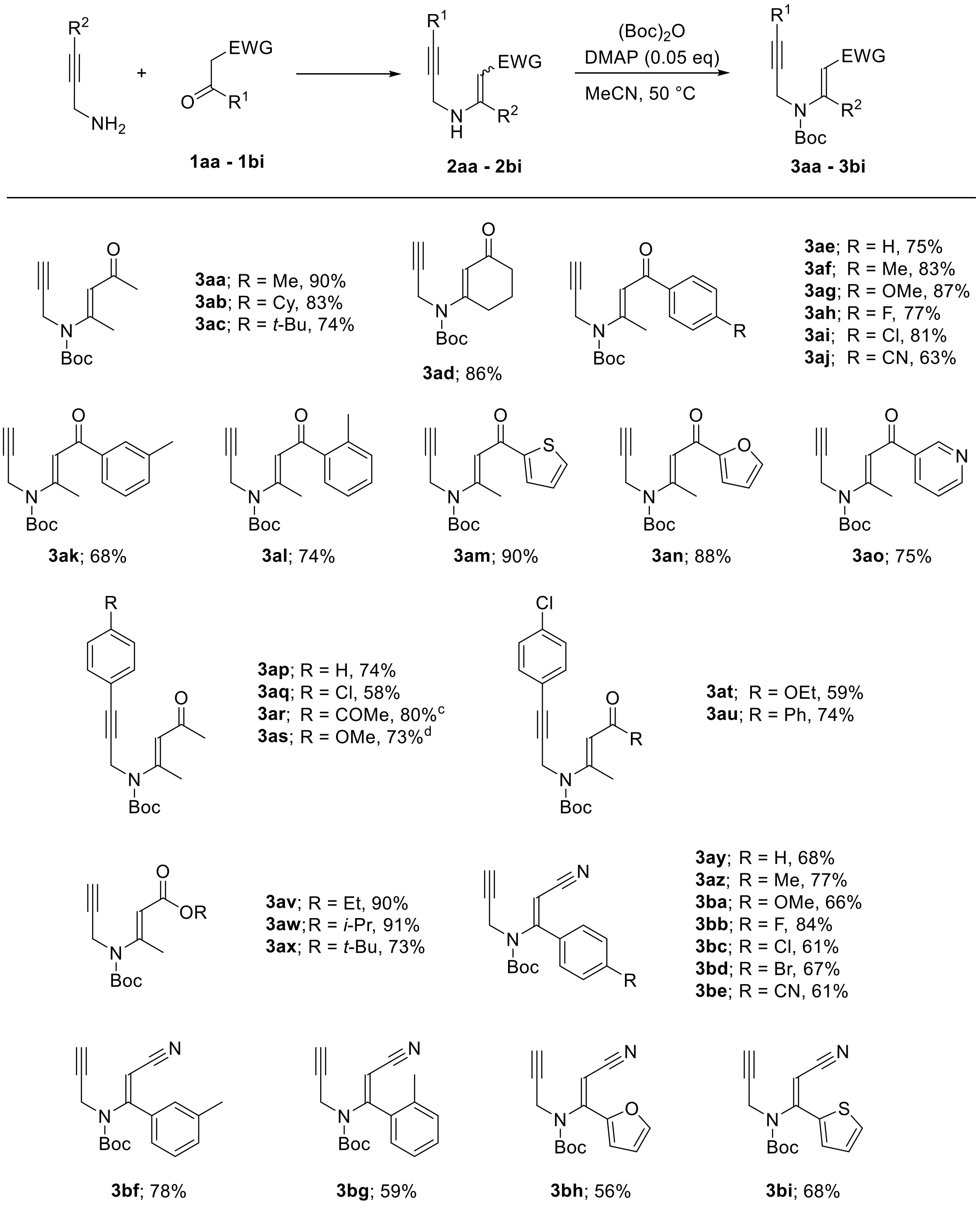


Figure 1. NOESY correlations of **3aa** and **3ay**



[a] Unless otherwise stated, reactions were performed with **1** (0.5-2 mmol) and propargylamine (1-5 eq). After evaporation, (Boc)$_2$O (1.2-2 eq) and DMAP (0.05 eq) were added to the crude products in MeCN at 50 °C.

[b] Isolated yield

[c] mixture of E and Z isomers (75:25) for **3ar** and (81:19) for **3as**

Scheme 2. Preparation of *N*-Boc-*N*-propargylenamines[a,b]

Next, we explored **3aa** as a model substrate for intramolecular cyclization. The reaction was carried out under various conditions. Attempts to cyclize the *N*-Boc-enamine **3aa** using either NaH, *n*-BuLi, or NaOMe as a base did not form the desired product (entries 1–3). Using NaOEt as a base, the cyclized and deprotected product **4aa** was obtained in 8% yield (entry 2). Surprisingly, even under basic conditions, NH-pyrrole **4aa** was obtained instead of *N*-Boc-pyrrole **5aa**. Some studies have reported on deprotection of *N*-Boc-heterocycles under basic conditions.[9] Considering this result, the reaction was carried out using *t*-BuOK as a base at room temperature to afford the product **4aa** in 94% yield (entry 3). The yield of the pyrrole derivative increased and the reaction was complete within 5 min at 70 °C (entry 4). Next, we investigated the effects of solvents on the intramolecular cyclization of **3aa** with *t*-BuOK (entries 5–10). The cyclized products were obtained in low to moderate yields, and *N*-Boc-pyrrole was isolated in a low yield (entries 7, 8, and 10).

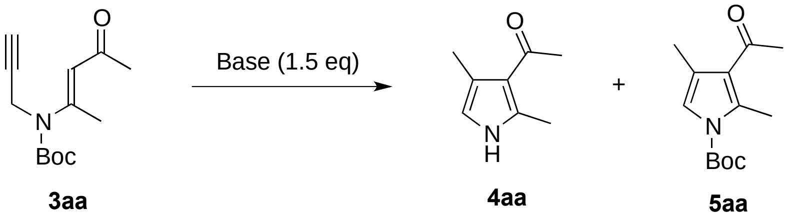
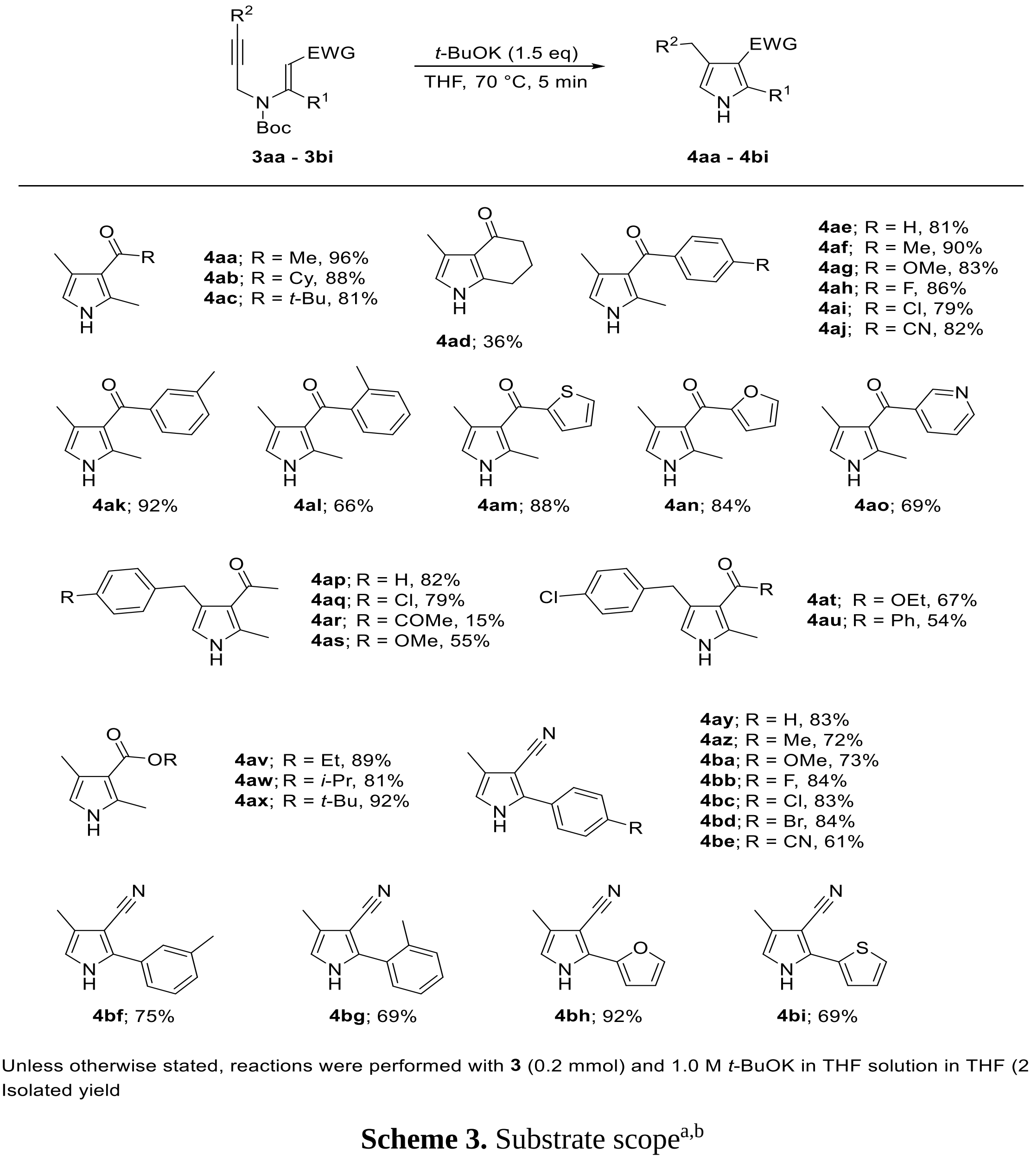


Table 1. Optimization of the reaction conditions[a]

Entry	Base	Solvent	Temp (°C)	Time (min)	Yield of **4aa** : **5aa** (%)[b]
1	NaOMe	THF	rt	30	0 : 0
2	NaOEt	THF	rt	30	8 : 0
3	*t*-BuOK	THF	rt	30	94 : 0
4	*t*-BuOK	THF	70	5	96 : 0
5	*t*-BuOK	1,4-dioxane	70	60	49 : 0
6	*t*-BuOK	Et_2O	reflux	90	42 : 0
7	*t*-BuOK	DME	70	1440	16 : 6
8	*t*-BuOK	MeCN	70	60	31 : 10
9	*t*-BuOK	toluene	70	90	53 : 0
10	*t*-BuOK	DCM	reflux	60	0 : 25

[a] Reaction Conditions: 0.1 M solvent under nitrogen atmosphere
[b] Yield of the isolated product

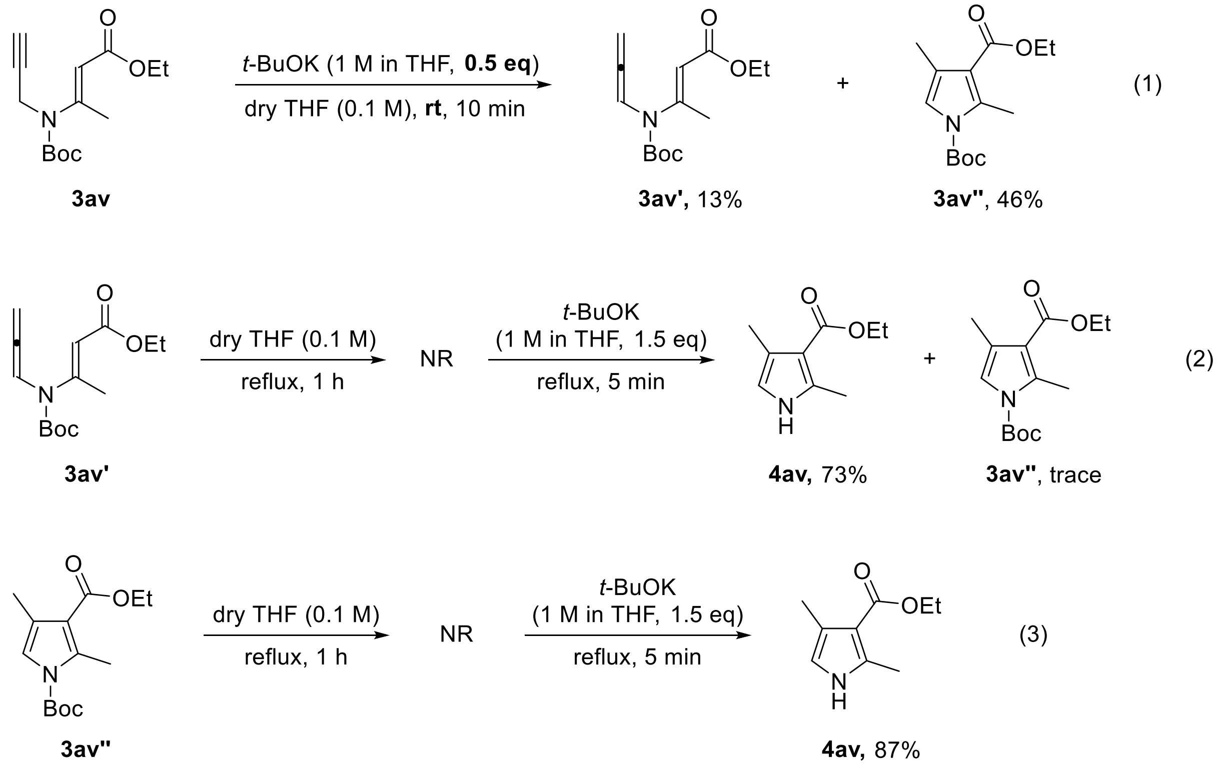
Using the optimum conditions (Table 1, entry 4), the generality of this reaction and the influences of various substituents on the intramolecular cyclization were examined (Scheme 3). The desired pyrroles were obtained in excellent yields from enaminones with primary, secondary, and tertiary alkyl groups (**4aa**–**4ac**). Tetrahydroindole derivative **4ad** was produced in only 36% yield from enaminone **3ad** containing a cyclic structure. Aromatic enaminones substituted at the *para*-position gave cyclized products in high yields, regardless of the substituent (e.g., neutral, electron donating, or electron withdrawing). The *ortho* isomer **4al** was obtained in relatively low yield compared with **4af**. Introduction of pyridine in place of a benzene ring caused a decrease in reactivity, whereas thiophene and furan substituents resulted in high yields (**4am**–**4ao**). When the cyclization was carried out with enaminone containing an internal alkyne structure, the yield decreased for **4ar** containing an electron withdrawing group, but pyrroles were obtained in moderate to high yields with other substituents (**4ap**, **4aq**, and **4as**–**4au**). When an enaminoester was used instead of an enaminone, the reaction proceeded in good yield under similar conditions. Varying the basic skeleton from a β-enaminone to a β-enaminoester allowed for the reaction to proceed in good yield under the same conditions. β-Cyanoenamines substituted with various aromatic rings were cyclized to give 3-cyanopyrrole derivatives. 2-Aryl-3-cyanopyrroles substituted at the *para*-position on aromatic ring were obtained in excellent yields in the presence of electron donating and halogen groups (**4ay**–**4bd**), whereas electron withdrawing groups resulted in moderate yields. The reactivity depended on the position of the substituent, with *meta* substitution giving a high yield and *ortho* substitution giving a moderate yield. With aromatic ring replaced by furan and thiophene, cyclized products were obtained in high and moderate yields, respectively.



[a] Unless otherwise stated, reactions were performed with **3** (0.2 mmol) and 1.0 M *t*-BuOK in THF solution in THF (2 mL).
[b] Isolated yield

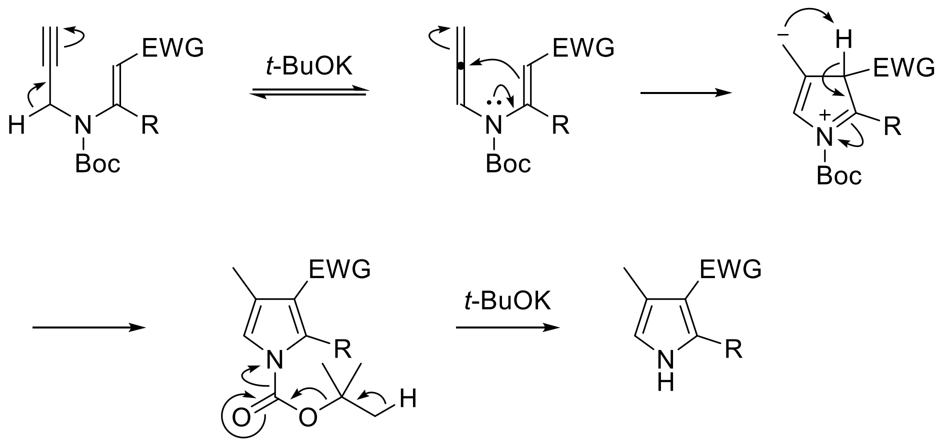
Scheme 3. Substrate scope[a,b]

To investigate the reaction mechanism, we designed three irregular experiments (Scheme 4). When the treatment of *N*-Boc-*N*-propargylenamine **3av** was carried out by reducing the amount of *t*-BuOK and lowering the temperature to room temperature as compared with the standard conditions, small amount of *N*-allenyl-*N*-Boc-enamine **3av'** and *N*-Boc-pyrrole **3av''** were obtained (1). Although **3av'** and **3av''**did not react without a base, respectively, cyclization of **3av'** readily provided **4av** and trace of **3av''** and deprotection of **3av''** readily provided **4av** in high yield under the standard conditions (2, 3). This implied that **3av'** and **3av''** are possible intermediates for the cyclization of **3av** to produce **4av**, and that base is indispensable for the formation of **4av**.



Scheme 4. Irregular experiments

On the basis of these results and similar reactions reported previously,[7c,7e] a plausible mechanism is illustrated in Scheme 5. First, *N*-Boc-*N*-propargylenamines **3** is isomerized to an allene in the presence of *t*-BuOK, and then an intramolecular 5-*exo-dig* cyclization occurs. Subsequently, after *N*-Boc-pyrrole is generated by proton transfer, the Boc group is decomposed by *t*-BuOK into isobutene and carbon dioxide to obtain *N*-H-pyrrole **4**.



Scheme 5. Plausible mechanism for cyclization of *N*-Boc-*N*-propargylenamines

In summary, we developed a 5-*exo-dig* cyclization of *N*-Boc-*N*-propargylenamines for the synthesis of 2,3,4-trisubstituted pyrroles. This methodology is environmentally benign because it does not use a transition metal. It is suitable for the synthesis of pyrrols bearing electron withdrawing groups, such as ketones, esters, and nitrile at the 3-position. The *N*-H-pyrroles obtained under basic conditions may be converted to various *N*-substituted pyrroles.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were measured on a Bruker BioSpin AVANCE III-400 spectrometer at 400 and 100 MHz, respectively. All NMR spectra were measured in $CDCl_3$. Chemical shifts were reported downfield from TMS (0 ppm) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported relative to $CDCl_3$ (77.2 ppm). Mass spectra were recorded on a JEOL JMS-T100LP mass spectrometer by electrospray ionization (ESI) and a JEOL JMS 600 mass spectrometer by chemical ionization (CI). Infrared spectra were measured on a Perkin-Elmer Spectrum Two. Purification was by column chromatography using 63–210 mm silica gel 60N (Kanto Chemical Co. Inc.). All melting points were measured with a Yanagimoto Micro melting point apparatus without collection. Unless otherwise noted, all materials were purchased from commercial sources, and commercially available reagents were used without further purification.

(*E*)-*tert*-Butyl 4-oxopent-2-en-2-yl(prop-2-yn-1-yl)carbamate (3aa)

Acetylacetone (0.21 mL, 2.0 mmol) and propargylamine (0.13 mL, 2.0 mmol) were stirred at rt for 2 h. The reaction mixture was evaporated to afford NH-enaminone **2aa** as a dark-red oil which was taken forward without further purification. To a solution of **2aa** and DMAP (12 mg, 0.10 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 2 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 6 : 1) to afford **3aa** as a yellow oil (0.43 g, 1.8 mmol, 90%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.50 (s, 9H), 2.23 (s, 3H), 2.30 (t, J = 2.4 Hz, 1H), 2.41 (d, J = 0.8 Hz, 3H), 4.27 (d, J = 2.4 Hz, 2H), 6.25 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 20.1, 27.9, 32.2, 39.0, 72.2, 79.0, 82.1, 117.1, 152.4, 155.0, 197.7; IR (film) cm^{-1}; 1591, 1710; HRMS (ESI+) *m/z*: [M+H]$^+$ Calcd for $C_{13}H_{20}NO_3$ 238.1443; Found 238.1450.

(*E*)-*tert*-Butyl 4-cyclohexyl-4-oxobut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ab)

1-Cyclohexylbutane-1,3-dione (0.34 g, 2.0 mmol) and propargylamine (0.13 mL, 2.0 mmol) were stirred at rt for 20 h. The reaction mixture was evaporated to afford NH-enaminone **2ab** as a dark-red oil which was taken forward without further purification. To a solution of **2ab** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added (Boc)$_2$O (0.92 mL, 4.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 2 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 8 : 1) to afford **3ab** as a yellow oil (508 mg, 1.66 mmol, 83%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.13–1.41 (m, 5H), 1.50 (s, 9H), 1.74–1.90 (m, 5H), 2.30 (t, J = 2.4 Hz, 1H), 2.31–2.39 (m, 1H), 2.37 (s, 3H), 4.27 (d, J = 2.4 Hz, 2H), 6.28 (d, J = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 20.3, 25.7, 25.9, 28.2, 28.6, 39.1, 52.2, 72.1, 79.3, 82.2, 116.8, 152.8, 155.0, 203.7; IR (film) cm^{-1}: 1590, 1711; HRMS (ESI+) *m/z*: [M+Na]$^+$ Calcd for $C_{18}H_{27}NNaO_3$ 328.1889; Found 328.1866.

(*E*)-*tert*-Butyl 5,5-dimethyl-4-oxohex-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ac)

5,5-Dimethylhexane-2,4-dione (0.14 g, 1.0 mmol) and propargylamine (0.13 mL, 2.0 mmol) were stirred at rt for 18 h. The reaction mixture was evaporated to afford NH-enaminone **2ac** as a dark-red oil which was taken forward without further purification. To a solution of **2ac** in MeCN (0.50 mL) was added (Boc)$_2$O (0.34 mL, 1.5 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 4 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 9 : 1) to afford **3ac** as a yellow oil (0.21 g, 0.74 mmol, 74%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.16 (s, 9H), 1.50 (s, 9H), 2.30 (t, J = 2.4 Hz, 1H), 2.36 (s, 3H), 4.27 (d, J = 2.4 Hz, 2H), 6.54 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 20.5, 26.6, 28.3, 39.2, 44.3, 72.2, 79.5, 82.3, 114.7, 153.0, 155.3, 205.9; IR (film) cm^{-1}: 1593, 1714; HRMS (ESI+) *m/z*: [M+Na]$^+$ Calcd for $C_{16}H_{25}NNaO_3$ 302.1732; Found 302.1710.

(*E*)-*tert*-Butyl 3-oxocyclohxenyl(prop-2-yn-1-yl)carbamate (3ad)[10]

To a solution of 1,3-cyclohexanedione (0.22 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.26 mL, 4.0 mmol) at rt and stirred for 24 h. The reaction mixture was evaporated to afford NH-enaminone **2ad** as a dark-red oil which was taken forward without further purification. To a solution of **2ad** and DMAP (12 mg, 0.10 mmol) in MeCN (1.0 mL) was added (Boc)$_2$O (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 2 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 2 : 1) to obtain **3ad** as a orange solid (0.42 g, 1.7 mmol, 86%). Mp 56−58 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.53 (s, 9H), 2.01 (quin, J = 6.2 Hz, 2H), 2.29 (t, J = 2.4 Hz, 1H), 2.40 (t, J = 6.2 Hz, 2H), 2.77 (t, J = 6.2 Hz, 2H), 4.31 (d, J = 2.4 Hz, 2H), 5.94 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 23.2, 28.2, 30.4, 36.9, 38.9, 72.7, 78.5, 83.3, 115.6, 151.9, 162.5, 199.5; IR (KBr) cm^{-1}: 1604, 1655, 1717; HRMS (ESI+) *m/z*: [M+H]$^+$ Calcd for $C_{14}H_{20}NO_3$ 250.1443; Found 250.1457.

(*E*)-*tert*-Butyl 4-oxo-4-phenylbut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ae)

To a solution of 1-phenyl-1,3-butanedione (0.32 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 16 h. The reaction mixture was evaporated to afford NH-enaminone **2ae** as a dark-red oil which was taken forward without further purification. To a solution of **2ae** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added (Boc)$_2$O (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 1) to afford **3ae** as a yellow oil (0.45 g, 1.5 mmol, 75%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.53 (s, 9H), 2.35 (t, *J* = 2.4 Hz, 1H), 2.50 (d, *J* = 0.7 Hz, 3H), 4.37 (d, *J* = 2.4 Hz, 2H), 6.98 (q, *J* = 0.7 Hz, 1H), 7.47 (t, *J* = 7.3 Hz, 2H), 7.55 (t, *J* = 1.3, 7.3 Hz, 1H), 7.92–7.96 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 20.7, 28.2, 39.3, 72.4, 79.4, 82.5, 114.8, 128.1, 128.6, 132.5, 139.5, 152.7, 156.5, 190.9; IR (film) cm^{-1}: 1600, 1660, 1713; HRMS (CI+) *m/z*: [M+H]$^+$ Calcd for $C_{18}H_{22}NO_3$ 300.1599; Found 300.1591.

(*E*)-*tert*-Butyl 4-oxo-4-*p*-tolylbut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3af)

To a solution of 1-*p*-tolylbutane-1,3-dione (0.35 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 19 h. The reaction mixture was evaporated to afford NH-enaminone **2af** as a dark-red oil which was taken forward without further purification. To a solution of **2af** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added (Boc)$_2$O (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 1) to afford **3af** as a yellow oil (0.52 g, 1.7 mmol, 83%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.53 (s, 9H), 2.34 (t, *J* = 2.4 Hz, 1H), 2.42 (s, 3H), 2.48 (d, *J* = 0.8 Hz, 3H), 4.36 (d, *J* = 2.4 Hz, 2H), 6.96 (d, *J* = 0.8 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 20.7, 21.8, 28.3, 39.4, 72.4, 79.5, 82.5, 115.4, 128.3, 129.4, 137.0, 143.4, 152.9, 155.9, 190.8; IR (film) cm^{-1}: 1580, 1654, 1732; HRMS (ESI+) *m/z*: [M+Na]$^+$ Calcd for $C_{19}H_{23}NNaO_3$ 336.1576; Found 336.1538.

(*E*)-*tert*-Butyl 4-(*p*-methoxyphenyl)-4-oxobut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ag)

To a solution of 1-(4-methoxyphenyl)butane-1,3-dione (0.38 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 18 h. The reaction mixture was evaporated to afford NH-enaminone **2ag** as a dark-red oil which was taken forward without further purification. To a solution of **2ag** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added (Boc)$_2$O (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 2) to afford **3ag** as a yellow oil (0.57 g, 1.7 mmol, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.35 (t, *J* = 2.4 Hz, 1H), 2.45 (d, *J* = 0.8 Hz, 3H), 3.88 (s, 3H), 4.36 (d, *J* = 2.4 Hz, 2H), 6.95 (q, *J* = 0.8 Hz, 1H), 6.95 (d, *J* = 9.0 Hz, 2H), 7.94 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.3, 28.1, 39.1, 55.3, 72.3, 79.4, 82.1, 113.6, 115.4, 130.2, 132.1, 152.7, 155.0, 163.0, 189.4; IR (film) cm^{-1}: 1601, 1709; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{23}NNaO_4$ 352.1525; Found 352.1483.

(*E*)-*tert*-Butyl 4-(*p*-fluorophenyl)-4-oxobut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ah)

To a solution of 1-(4-fluorophenyl)butane-1,3-dione (0.36 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 20 h. The reaction mixture was evaporated to afford NH-enaminone **2ah** as a dark-red oil which was taken forward without further purification. To a solution of **2ah** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 1) to afford **3ah** as a yellow oil (0.49 g, 1.5 mmol, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.36 (t, *J* = 2.5 Hz, 1H), 2.49 (d, *J* = 0.8 Hz, 3H), 4.37 (d, *J* = 2.5 Hz, 2H), 6.94 (d, *J* = 0.8 Hz, 1H), 7.13 (t, *J* = 8.8 Hz, 2H), 7.97 (dd, *J* = 5.4, 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7, 28.2, 39.3, 72.5, 79.4, 82.7, 114.3, 115.6 (d, *J* = 21.7 Hz), 130.7 (d, *J* = 9.3 Hz), 135.9 (d, *J* = 2.9 Hz), 152.7, 156.8, 165.4 (d, *J* = 253.8 Hz), 189.4; IR (film) cm^{-1}: 1599, 1712; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{20}FNNaO_3$ 340.1325; Found 340.1317.

(*E*)-*tert*-Butyl 4-(*p*-chlorophenyl)-4-oxobut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ai)

To a solution of 1-(4-chlorophenyl)butane-1,3-dione (0.39 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 20 h. The reaction mixture was evaporated to afford NH-enaminone **2ai** as a dark-red oil which was taken forward without further purification. To a solution of **2ai** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 1) to afford **3ai** as a yellow oil (0.54 g, 1.6 mmol, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.37 (t, *J* = 2.4 Hz, 1H), 2.51 (s, 3H), 4.37 (d, *J* = 2.4 Hz, 2H), 6.93 (s, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.88 (d, *J* = 8.5 Hz 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8, 28.2, 39.4, 72.5, 79.3, 82.7, 113.8, 128.9, 129.5, 137.9, 138.8, 152.6, 157.3, 189.6; IR (film) cm^{-1}: 1577, 1732; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{20}ClNNaO_3$ 356.1029; Found 356.1025.

(*E*)-*tert*-Butyl 4-(*p*-cyanophenyl)-4-oxobut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3aj)

To a solution of 4-(3-oxobutanoyl)benzonitrile (0.37 g, 2.0 mmol) and molecular sieve 4A (0.72 g) in CH_2Cl_2 (2.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 24 h. The reaction mixture was evaporated to afford NH-enaminone **2aj** as a dark-red oil which was taken forward without further purification. To a solution of **2aj** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added

$(Boc)_2O$ (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 4 : 1) to afford **3aj** as a yellow solid (0.41 g, 1.3 mmol, 63%). Mp 108−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 9H), 2.38 (t, *J* = 2.4 Hz, 1H), 2.56 (d, *J* = 0.5 Hz, 3H), 4.39 (d, *J* = 2.4 Hz, 2H), 6.94 (d, *J* = 0.5 Hz, 1H), 7.77 (d, *J* = 8.6 Hz, 2H), 8.00 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 28.3, 39.5, 72.8, 79.2, 83.3, 112.4, 115.6, 118.3, 128.5, 132.6, 143.1, 152.5, 159.1, 189.2; IR (KBr) cm^{-1}: 1571, 1651, 1724, 2229; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{20}N_2NaO_3$ 347.1372; Found 347.1362.

(*E*)-*tert*-Butyl 4-oxo-4-*m*-tolylbut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ak)

1-*m*-Tolylbutane-1,3-dione (0.35 g, 2.0 mmol) and propargylamine (1.3 mL, 20 mmol) was stirred at rt for 18 h. The reaction mixture was evaporated to afford NH-enaminone **2ak** as a dark-red oil which was taken forward without further purification. To a solution of **2ak** and DMAP (12 mg, 0.10 mmol) in CH_2Cl_2 (2.0 mL) was added $(Boc)_2O$ (0.92 mL, 4.0 mmol) under nitrogen atmosphere, and then stirred at rt for 14 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt/DCM 16 : 1 : 4) to afford **3ak** as a yellow oil (0.43 g, 1.4 mmol, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.35 (t, *J* = 2.4 Hz, 1H), 2.42 (s, 3H), 2.49 (d, *J* = 0.5 Hz, 3H), 4.37 (d, *J* = 2.4 Hz, 2H), 6.96 (d, *J* = 0.5 Hz, 1H), 7.33−7.38 (m, 2H), 7.70−7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7, 21,5, 28.3, 39.3, 72.4, 79.4, 82.5, 115.2, 125.3, 128.5, 128.7, 133.3, 138.3, 139.5, 152.8, 156.1, 191.2; IR (film) cm^{-1}: 1586, 1661, 1711; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{23}NNaO_3$ 336.1576; Found 336.1542.

(*E*)-*tert*-Butyl 4-oxo-4-*o*-tolylbut-2-en-2-yl(prop-2-yn-1-yl)carbamate (3al)

1-*o*-Tolylbutane-1,3-dione (0.35 g, 2.0 mmol) and propargylamine (1.3 mL, 20 mmol) was stirred at rt for 18 h. The reaction mixture was evaporated to afford NH-enaminone **2al** as a dark-red oil which was taken forward without further purification. To a solution of **2al** and DMAP (12 mg, 0.10 mmol) in CH_2Cl_2 (2.0 mL) was added $(Boc)_2O$ (0.92 mL, 4.0 mmol) under nitrogen atmosphere, and then stirred at rt for 10 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt/DCM 12 : 1 : 4) to afford **3al** as a yellow oil (0.46 g, 1.5 mmol, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.55 (s, 9H), 2.32 (t, *J* = 2.4 Hz, 1H), 2.49 (d, *J* = 0.7 Hz, 3H), 2.52 (s, 3H), 4.35 (d, *J* = 2.4 Hz, 2H), 6.64 (d, *J* = 0.7 Hz, 1H), 7.24−7.33 (m, 2H), 7.34−7.39 (m, 1H), 7.55−7.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.6, 20.7, 28.2, 39.2, 72.4, 79.3, 82.5, 118.2, 125.7, 128.3, 130.7, 131.5, 137.2, 140.7, 152.7, 155.8, 195.2; IR (film) cm^{-1}: 1580, 1662, 1711; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{23}NNaO_3$ 336.1576; Found 336.1512.

(*E*)-*tert*-Butyl 4-oxo-4-(thiophen-2-yl)but-2-en-2-yl(prop-2-yn-1-yl)carbamate (3am)

To a solution of 1-(thiophen-2-yl)butane-1,3-dione (0.34 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 16 h. The reaction mixture was evaporated to afford NH-enaminone **2am** as a dark-red oil which was taken forward without further purification. To a solution of **2am** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 1) to afford **3am** as a yellow oil (0.55 g, 1.8 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.37 (t, *J* = 2.4 Hz, 1H), 2.53 (d, *J* = 0.7 Hz, 3H), 4.37 (d, *J* = 2.4 Hz, 2H), 6.92 (d, *J* = 0.7 Hz, 1H), 7.13 (dd, *J* = 3.8, 4.9 Hz, 1H), 7.61 (dd, *J* = 1.1, 4.9 Hz, 1H), 7.69 (dd, *J* = 1.1, 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8, 28.3, 39.5, 72.5, 79.4, 82.7, 113.8, 128.2, 130.8, 133.3, 147.4, 152.7, 157.1, 183.0; IR (film) cm^{-1}: 1584, 1645, 1711; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{19}NNaO_3S$ 328.0983; Found 328.0963.

(*E*)-*tert*-Butyl 4-(furan-2-yl)-4-oxo-but-2-en-2-yl(prop-2-yn-1-yl)carbamate (3an)

To a solution of 1-(furan-2-yl)butane-1,3-dione (0.30 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 18 h. The reaction mixture was evaporated to afford NH-enaminone **2an** as a dark-red oil which was taken forward without further purification. To a solution of **2an** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 2) to afford **3an** as a yellow oil (0.51 g, 1.8 mmol, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52 (s, 9H), 2.34 (t, *J* = 2.4 Hz, 1H), 2.56 (d, *J* = 0.7 Hz, 3H), 4.37, (d, *J* = 2.4 Hz, 2H), 6.53 (dd, *J* = 1.7, 3.5 Hz, 1H), 6.89, (d, *J* = 0.7 Hz, 1H), 7.17 (dd, *J* = 0.7, 3.5 Hz, 1H), 7.58 (dd, *J* = 0.7, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 28.2, 39.4, 72.4, 79.3, 82.7, 112.3, 112.9, 116.2, 146.0, 152.7, 154.6, 157.5, 178.9; IR (film) cm^{-1}: 1587, 1657, 1712; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{19}NNaO_4$ 312.1212; Found 312.1190.

(*E*)-*tert*-Butyl 4-oxo-4-(pyridin-3-yl)but-2-en-2-yl(prop-2-yn-1-yl)carbamate (3ao)

To a solution of 1-(pyridin-3-yl)butane-1,3-dione (0.33 g, 2.0 mmol) in EtOH (1.0 mL) was added propargylamine (0.64 mL, 10 mmol) at rt and stirred for 18 h. The reaction mixture was evaporated to afford NH-enaminone **2ao** as a dark-red oil which was taken forward without further purification. To a solution of **2ao** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.55 mL, 2.4 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 1 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 3 : 2) to afford **3ao** as a yellow oil (0.45 g, 1.5 mmol, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 9H), 2.38 (t, *J* = 2.4 Hz, 1H), 2.57 (d, *J* = 0.3 Hz, 3H), 4.40 (d, *J* = 2.4 Hz, 2H), 6.98 (d, *J* = 0.3 Hz, 1H), 7.42 (ddd, *J* = 0.6, 4.8, 8.0 Hz, 1H), 8.22 (dt, *J* = 2.0, 8.0 Hz, 1H), 8.75 (dd, *J* = 2.0, 4.8 Hz, 1H), 9.15 (dd, *J* = 0.6, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 28.2, 39.4, 72.7, 79.1, 83.0, 112.5, 123.6, 134.9, 135.5, 149.3, 152.5, 152.7, 158.5, 189.0; IR (film) cm^{-1}: 1587, 1714; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{20}N_2NaO_3$ 323.1372; Found 323.1355.

(*E*)-*tert*-Butyl (4-oxopent-2-en-2-yl)(3-phenylprop-2-yn-1-yl)carbamate (3ap)

To a solution of 3-phenylprop-2-yn-1-amine hydrogen chloride (0.25 g, 1.5 mmol) in EtOH (1.0 mL) was added acetylacetone (0.10 mL, 1.0 mmol) and triethylamine (0.42 mL, 3.0 mmol) at rt and stirred for 18 h. The resulting solution was quenched by saturated NH_4Cl aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-enaminone **2ap** as a yellow oil which was taken forward without further purification. To a solution of **2ap** and DMAP (6.1 mg, 0.050 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.46 mL, 2.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 2 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 6 : 1) to afford **3ap** as a yellow solid (0.23 g, 0.74 mmol, 74%). Mp 61−63 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 1.52 (s, 9H), 2.24 (s, 3H), 2.45 (d, J = 0.7 Hz, 3H), 4.50 (s, 2H), 6.33 (s, 1H), 7.29−7.34 (m, 3H), 7.39−7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.3, 28.2, 32.4, 40.0, 82.3, 83.9, 84.6, 117.4, 122.5, 128.3, 128.5, 131.6, 152.8, 155.3, 198.0; IR (KBr) cm^{-1}: 1590, 1714; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{23}NNaO_3$ 336.1576; Found 336.1585.

(*E*)-*tert*-Butyl (3-(4-chlorophenyl)prop-2-yn-1-yl)(4-oxopent-2-en-2-yl)carbamate (3aq)

To a solution of 3-(4-chlorophenyl)prop-2-yn-1-amine (0.17 g, 1.0 mmol) in EtOH (1.0 mL) was added acetylacetone (0.11 mL, 1.1 mmol) at rt and stirred for 8 h. The reaction mixture was evaporated to afford NH-enaminone **2aq** as a dark-red oil which was taken forward without further purification. To a solution of **2aq** and DMAP (67 mg, 0.55 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (1.1 mL, 5.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 6 h. The residue was purified by column chromatography with silica gel ($CHCl_3$/*n*-hexane/AcOEt 1 : 2 : 0.1) to afford **3aq** as a yellow solid (0.20 g, 0.58 mmol, 58%). Mp 74−76 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 1.52 (s, 9H), 2.24 (s, 3H), 2.44 (d, J = 0.6 Hz, 3H), 4.49 (s, 2H), 6.29 (s, 1H), 7.29 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.3, 28.2, 32.4, 40.0, 82.3, 82.8, 85.6, 117.5, 121.0, 128.7, 132.9, 134.5, 152.7, 155.2, 198.0; IR (KBr) cm^{-1}: 1590, 1714; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{23}ClNO_3$ 348.1367; Found 348.1373.

(*E*)-*tert*-Butyl (3-(4-acetylphenyl)prop-2-yn-1-yl)(4-oxopent-2-en-2-yl)carbamate (3ar)

To a solution of 1-(4-(3-aminoprop-1-yn-1-yl)phenyl)ethan-1-one (0.17 g, 1.0 mmol) in EtOH (1.0 mL) was added acetylacetone (0.11 mL, 1.1 mmol) at rt and stirred for 6 h. The reaction mixture was evaporated to afford NH-enaminone **2ar** as a dark-red oil which was taken forward without further purification. To a solution of **2ar** and DMAP (61 mg, 0.50 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.46 mL, 2.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 4 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 3 : 1) to afford **3ar** as a isomer mixture (*E* : *Z* = 75 : 25) as a yellow oil (0.29 g, 0.81 mmol, 80%). ^1H NMR (400 MHz, $CDCl_3$, (*E*)−**3ar**):

δ 1.52 (s, 9H), 2.24 (s, 3H), 2.44−2.45 (m, 3H), 2.60 (s, 3H), 4.52 (s, 2H), 6.30 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.91 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, (*E*) and (*Z*)−**3ar**): δ 20.1, 22.8, 26.4, 28.0, 30.5, 32.2, 37.8, 39.8, 81.2, 82.2, 83.0, 87.9, 88.1, 117.4, 124.1, 127.1, 127.3, 128.1, 131.5, 131.6, 136.1, 136.2, 148.3, 152.4, 152.5, 155.0, 196.0, 196.9, 197.7; IR (film) cm^{-1}: 1597, 1682; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{26}NO_4$ 356.1862; Found 356.1873.

(*E*)-*tert*-Butyl (3-(4-methoxyphenyl)prop-2-yn-1-yl)(4-oxopent-2-en-2-yl)carbamate (3as)

To a solution of 3-(4-methoxyphenyl)prop-2-yn-1-amine (0.16 g, 1.0 mmol) in EtOH (1.0 mL) was added acetylacetone (0.11 mL, 1.1 mmol) at rt and stirred for 24 h. The reaction mixture was evaporated to afford NH-enaminone **2as** as a dark-red oil which was taken forward without further purification. To a solution of **2as** and DMAP (61 mg, 0.50 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.46 mL, 2.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 2 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 5 : 1) to afford **3as** as a isomer mixture (*E* : *Z* = 81 : 19) as a yellow oil (0.25 g, 0.73 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$, (*E*)−**3as**): δ 1.52 (s, 9H), 2.24 (s, 3H), 2.44 (d, *J* = 8.9 Hz, 3H), 3.81 (s, 3H), 4.48 (s, 2H), 6.33 (s, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 7.34 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, (*E*) and (*Z*)−**3as**): δ 20.3, 22.9, 28.1, 28.2, 30.4, 32.4, 37.9, 40.1, 55.2, 81.2, 82.2, 83.0, 83.1, 83.8, 84.0, 113.9, 113.9, 114.6, 114.7, 117.3, 124.6, 133.0, 133.1, 148.6, 152.6, 152.8, 155.3, 159.6, 159.7, 196.4, 198.0; IR (film) cm^{-1}: 1614, 1705; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{25}NNaO_4$ 366.1681; Found 366.1699.

(*E*)-Ethyl 3-((*tert*-butoxycarbonyl)(3-(4-chlorophenyl)prop-2-yn-1-yl)amino)but-2-enoate (3at)

To a solution of 3-(4-chlorophenyl)prop-2-yn-1-amine (0.17 g, 1.0 mmol) in EtOH (1.0 mL) was added ethyl acetoacetate (0.14 mL, 1.1 mmol) at rt and stirred for 15 h. The reaction mixture was evaporated to afford NH-enaminoester **2at** as a dark-red oil which was taken forward without further purification. To a solution of **2at** and DMAP (61 mg, 0.50 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.57 mL, 2.5 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 5 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 10 : 1) to afford **3at** as a yellow oil (0.22 g, 0.59 mmol, 59%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, *J* = 7.1 Hz, 3H), 1.51 (s, 9H), 2.45 (d, *J* = 0.8 Hz, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.47 (s, 2H), 5.88−5.91 (m, 1H), 7.28 (d, *J* = 8.6 Hz, 2H), 7,34 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 19.8, 28.2, 40.0, 59.9, 82.1, 82.8, 85.7, 111.7, 121.1, 128.6, 132.9, 134.4, 152.7, 156.4, 166.8; IR (film) cm^{-1}: 1634, 1714; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{20}H_{24}ClNNaO_4$ 400.1292; Found 400.1289.

***tert*-Butyl (*E*)-(3-(4-chlorophenyl)prop-2-yn-1-yl)(4-oxo-4-phenylbut-2-en-2-yl)carbamate (3au)**

To a solution of 3-(4-chlorophenyl)prop-2-yn-1-amine (0.17 g, 1.0 mmol) in EtOH (1.0 mL) was added 1-phenyl-1,3-butanedione (0.26 g, 1.6 mmol) at rt and stirred for 15 h. The reaction mixture was evaporated to afford NH-enaminone **2au** as a dark-red oil which was taken forward without further purification. To a solution of **2au** and DMAP (61 mg, 0.50 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.57 mL, 2.5 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 2 h. The residue was purified by column chromatography with silica gel (CH_2Cl_2/*n*-hexane/AcOEt 1 : 2 : 0.1) to afford **3au** as a yellow solid (0.31 g, 0.74 mmol, 74%). Mp 64−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 9H), 2.52 (d, *J* = 0.7 Hz, 3H), 4.58 (s, 2H), 7.05−7.06 (m, 1H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 7.39−7.45 (m, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.6, 28.2, 39.9, 82.4, 83.0, 85.8, 115.1, 121.0, 128.0, 128.5, 128.7, 132.5, 132.9, 134.6, 139.4, 152.8, 156.3, 190.9; IR (KBr) cm^{-1}: 1660, 1715; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{25}ClNO_3$ 410.1523; Found 410.1530.

(*E*)-Ethyl 3-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)but-2-enoate (3av)

Ethyl 3-oxobutanoate (0.26 mL, 2.0 mmol) and propargylamine (0.38 mL, 6.0 mmol) were stirred at rt for 2 h. The reaction mixture was evaporated to afford NH-enaminoester **2av** as a dark-red oil which was taken forward without further purification. To a solution of **2av** and DMAP (12 mg, 0.10 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.69 mL, 3.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 3 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 7 : 1) to afford **3av** as a yellow oil (0.49 g, 1.8 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, *J* = 7.1 Hz, 3H), 1.50 (s, 9H), 2.28 (t, *J* = 2.4 Hz, 1H), 2.43 (d, *J* = 0.9 Hz, 3H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.26 (d, *J* = 2.4 Hz, 2H), 5.85 (q, *J* = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 19.7, 28.1, 39.2, 59.8, 72.2, 79.2, 82.1, 111.4, 152.6, 156.4, 166,7; IR (film) cm^{-1}: 1627, 1711; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{21}NNaO_4$ 290.1368; Found 290.1359.

(*E*)-*iso*-Propyl 3-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)but-2-enoate (3aw)

iso-Propyl 3-oxobutanoate (0.29 mL, 2.0 mmol) and propargylamine (0.38 mL, 6.0 mmol) were stirred at rt for 2 h. The reaction mixture was evaporated to afford NH-enaminoester **2aw** as a dark-red oil which was taken forward without further purification. To a solution of **2aw** and DMAP (12 mg, 0.10 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.92 mL, 4.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 4 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 8 : 1) to afford **3aw** as a yellow oil (0.51 g, 1.8 mmol, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (d, *J* = 6.2 Hz, 6H), 1.50 (s, 9H), 2.28 (t, *J* = 2.4 Hz, 1H), 2.42 (d, *J* = 0.9 Hz, 3H), 4.25 (d, *J* = 2.4 Hz, 2H), 5.05 (septet, *J* = 6.2 Hz, 1H), 5.82 (q, *J* = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 22.0, 28.2, 39.3, 67.1, 72.2, 79.3, 82.1, 112.1, 152.7, 156.2, 166.3; IR (film) cm^{-1}: 1627, 1711; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{23}NNaO_4$ 304.1525; Found 304.1514.

(*E*)-*tert*-Butyl 3-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)but-2-enoate (3ax)

tert-Butyl 3-oxobutanoate (0.33 mL, 2.0 mmol) and propargylamine (0.38 mL, 6.0 mmol) were stirred at rt for 2 h. The reaction mixture was evaporated to afford NH-enaminoester **2ax** as a dark-red oil which was taken forward without further purification. To a solution of **2ax** and DMAP (12 mg, 0.10 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (1.4 mL, 6.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 12 h. The residue was purified by column chromatography with silica gel (*n*-hexane/AcOEt 10 : 1) to afford **3ax** as a yellow oil (0.44 g, 1.5 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.49 (s, 9H), 1.50 (s, 9H), 2.28 (t, J = 2.4 Hz, 1H), 2.38 (d, J = 0.9 Hz, 3H), 4.23 (d, J = 2.4 Hz, 2H), 5.78 (q, J = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.6, 28.2, 28.3, 39.4, 72.1, 79.4, 80.1, 82.0, 113.9, 152.8, 155.3, 166.2; IR (film) cm^{-1}: 1626, 1709; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{25}NNaO_4$ 318.1681; Found 318.1669.

(*E*)-*tert*-Butyl (2-cyano-1-phenylvinyl)(prop-2-yn-1-yl)carbamate (3ay)

To a solution of 3-oxo-3-phenylpropanenitrile (0.073 g, 0.50 mmol) in AcOH (0.75 mL) was added propargylamine (0.096 mL, 1.5 mmol) at 50 °C and stirred for 17 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2ay** as a yellow oil which was taken forward without further purification. To a solution of **2ay** and DMAP (3.1 mg, 0.025 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.14 mL, 0.60 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 2 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 3 : 1) to afford **3ay** as a yellow oil (0.095 g, 0.34 mmol, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (s, 9H), 2.39 (t, J = 2.5 Hz, 1H), 4.45 (d, J = 2.5 Hz, 2H), 5.54 (s, 1H), 7.40−7.49, (m, 3H), 7.50−7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.6, 39.9, 73.3, 78.3, 83.2, 88.0, 117.6, 128.0, 128.6, 130.7, 135.5, 152.2, 160.1; IR (film) cm^{-1}: 1717, 2216.

(*E*)-*tert*-Butyl (2-cyano-1-(*p*-tolyl)vinyl)(prop-2-yn-1-yl)carbamate (3az)

To a solution of 3-oxo-3-(*p*-tolyl)propanenitrile (0.080 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 5 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2az** as a yellow oil which was taken forward without further purification. To a solution of **2az** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 21 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 4 : 1) to afford **3az** as a yellow oil (0.11 g, 0.39 mmol, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (s, 9H), 2.36 (t, J = 2.4 Hz, 1H), 2.39 (s, 3H), 4.40 (d, J = 2.4 Hz, 2H), 5.50 (s, 1H), 7.23 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 27.6, 39.8, 73.1, 78.4, 83.0, 87.7, 117.7, 127.9, 129.2, 132.5, 141.0, 152.3, 160.1; IR (film) cm^{-1}: 1716, 2215.

(*E*)-*tert*-Butyl (2-cyano-1-(4-methoxyphenyl)vinyl)(prop-2-yn-1-yl)carbamate (3ba)

To a solution of 3-(4-methoxyphenyl)-3-oxopropanenitrile (0.090 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 7 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2ba** as a yellow oil which was taken forward without further purification. To a solution of **2ba** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 13 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 2 : 1) to afford **3ba** as a yellow oil (0.11 g, 0.34 mmol, 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (s, 9H), 2.36 (t, *J* = 2.4 Hz, 1H), 3.85 (s, 3H), 4.40 (d, *J* = 2.4 Hz, 2H), 5.46 (s, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.8, 39.9, 55.5, 73.1, 78.5, 83.0, 87.3, 114.0, 118.0, 127.7, 129.7, 152.4, 159.8, 161.6; IR (film) cm^{-1}: 1714, 2212; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{20}N_2NaO_3$ 335.1372; Found 335.1369.

(*E*)-*tert*-Butyl (2-cyano-1-(4-fluorophenyl)vinyl)(prop-2-yn-1-yl)carbamate (3bb)

To a solution of 3-(4-fluorophenyl)-3-oxopropanenitrile (0.083 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 4 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2bb** as a yellow oil which was taken forward without further purification. To a solution of **2bb** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 14 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 4 : 1) to afford **3bb** as a yellow oil (0.13 g, 0.43 mmol, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (s, 9H), 2.38 (t, *J* = 2.4 Hz, 1H), 4.43 (d, *J* = 2.4 Hz, 2H), 5.53 (s, 1H), 7.14 (t, *J* = 8.7 Hz, 2H), 7.54 (dd, *J* = 5.2, 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.6, 39.9, 73.4, 78.2, 83.3, 88.2, 115.8 (d, *J* = 22.1 Hz), 117.4, 130.1 (d, *J* = 8.7 Hz), 131.6 (d, *J* = 3.4 Hz), 152.0, 159.0, 163.9 (d, *J* = 251.6 Hz); IR (film) cm^{-1}: 1714, 2217.

(*E*)-*tert*-Butyl (1-(4-chlorophenyl)-2-cyanovinyl)(prop-2-yn-1-yl)carbamate (3bc)

To a solution of 3-(4-chlorophenyl)-3-oxopropanenitrile (0.078 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.32 mL, 5.0 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 7 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2bc** as a yellow oil which was taken forward without further purification. To a solution of **2bc** and DMAP (3.1 mg, 0.025 mmol) in MeCN (1.0 mL) was added $(Boc)_2O$ (0.14 mL, 0.60 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 3 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 3 : 1) to afford **3bc** as a yellow oil (0.093 g, 0.29 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (s, 9H), 2.38 (t, *J* = 2.5 Hz, 1H), 4.44 (d, *J* = 2.5 Hz, 2H), 5.54 (s, 1H), 7.42 (d, *J* = 6.6 Hz, 2H), 7.48 (d, *J* = 6.6 Hz, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.7, 39.9, 73.5, 78.1, 83.6, 88.5, 117.3, 129.0, 129.4, 134.0, 136.7, 152.0, 158.9; IR (film) cm^{-1}: 1723, 2212. HRMS (ESI−) *m/z*: $[M-H]^+$ Calcd for $C_{17}H_{16}ClN_2O_2$ 315.0900; Found 315.0913.

(*E*)-*tert*-Butyl (1-(4-bromophenyl)-2-cyanovinyl)(prop-2-yn-1-yl)carbamate (3bd)

To a solution of 3-(4-bromophenyl)-3-oxopropanenitrile (0.12 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 3 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2bd** as a yellow oil which was taken forward without further purification. To a solution of **2bd** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 24 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 4 : 1) to afford **3bd** as a yellow oil (0.13 g, 0.36 mmol, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (s, 9H), 2.38 (t, *J* = 2.4 Hz, 1H), 4.43 (d, *J* = 2.4 Hz, 2H), 5.54 (s, 1H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.7, 39.9, 73.5, 78.1, 83.6, 88.4, 117.3, 125.0, 129.5, 131.9, 134.5, 151.9, 158.9; IR (film) cm^{-1}: 1715, 2217.

(*E*)-*tert*-Butyl (2-cyano-1-(4-cyanophenyl)vinyl)(prop-2-yn-1-yl)carbamate (3be)

To a solution of 4-(2-cyanoacetyl)benzonitrile (0.086 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 3 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2be** as a yellow oil which was taken forward without further purification. To a solution of **2be** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 17 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 3 : 2) to afford **3be** as a yellow oil (0.095 g, 0.31 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (s, 9H), 2.43 (t, *J* = 2.4 Hz, 1H), 4.48 (d, *J* = 2.4 Hz, 2H), 5.62 (s, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.6, 39.9, 73.8, 77.7, 84.0, 89.4, 113.9, 116.7, 118.0, 128.6, 132.3, 140.1, 151.4, 157.9; IR (film) cm^{-1}: 1720, 2219, 2230; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{18}H_{16}N_3O_2$ 306.1243; Found 306.1257.

(*E*)-*tert*-Butyl (2-cyano-1-(*m*-tolyl)vinyl)(prop-2-yn-1-yl)carbamate (3bf)

To a solution of 3-oxo-3-(*m*-tolyl)propanenitrile (0.080 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 5 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2bf** as a yellow oil which was taken forward without further purification. To a solution of **2bf** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 15 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 4 : 1) to afford **3bf** as a yellow oil (0.12 g, 0.39 mmol, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (s, 9H), 2.37 (t, *J* = 2.4 Hz, 1H), 2.38 (s, 3H), 4.42 (d, *J* = 2.4 Hz, 2H), 5.52 (s, 1H), 7.24−7.37 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 27.6, 39.9, 73.2, 78.4, 83.1, 87.8, 117.7, 125.3, 128.5, 128.6, 131.4, 135.4, 138.4, 152.3, 160.2; IR (film) cm^{-1}: 1716, 2216; HRMS (ESI+) *m/z*: [M+Na]$^+$ Calcd for $C_{18}H_{20}N_2NaO_2$ 319.1423; Found 319.1454.

(*E*)-*tert*-Butyl (2-cyano-1-(*o*-tolyl)vinyl)(prop-2-yn-1-yl)carbamate (3bg)

To a solution of 3-oxo-3-(*o*-tolyl)propanenitrile (0.080 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 20 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2bg** as a yellow oil which was taken forward without further purification. To a solution of **2bg** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 3 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 6 : 1) to afford **3bg** as a yellow oil (0.089 g, 0.30 mmol, 59%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (s, 9H), 2.33−2.36(m, 4H), 4.34 (d, *J* = 2.4 Hz, 2H), 5.65 (s, 1H), 7.20−7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.6, 27.7, 38.9, 73.1, 78.2, 83.6, 87.8, 117.5, 126.1, 129.0, 130.0, 130.9, 134.9, 136.2, 152.1, 159.1; IR (film) cm^{-1}: 1716, 2216; HRMS (ESI+) *m/z*: [M+Na]$^+$ Calcd for $C_{18}H_{20}N_2NaO_2$ 319.1423; Found 319.1437.

(*E*)-*tert*-Butyl (2-cyano-1-(furan-2-yl)vinyl)(prop-2-yn-1-yl)carbamate (3bh)

To a solution of 3-(furan-2-yl)-3-oxopropanenitrile (0.069 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 5 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2bh** as a yellow oil which was taken forward without further purification. To a solution of **2bh** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 19 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 5 : 1) to afford **3bh** as a yellow oil (0.078 g, 0.28 mmol, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 9H), 2.35 (t, *J* = 2.5 Hz, 1H), 4.36 (d, *J* = 2.5 Hz, 2H), 5.46 (s, 1H), 6.55 (dd, *J* = 1.7, 3.6 Hz, 1H), 7.06 (dd, *J* = 0.6, 3.6 Hz, 1H), 7.54 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.9, 39.6, 73.3, 78.6, 82.9, 87.8, 112.6, 115.1, 117.0, 144.4, 147.9, 148.1, 152.4; IR (film) cm^{-1}: 1715, 2215; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{16}N_2NaO_3$ 295.1059; Found 295.1010.

(*E*)-*tert*-Butyl (2-cyano-1-(thiophen-2-yl)vinyl)(prop-2-yn-1-yl)carbamate (3bi)

To a solution of 3-oxo-3-(thiophen-2-yl)propanenitrile (0.076 g, 0.50 mmol) in EtOH (5.0 mL) was added propargylamine (0.16 mL, 2.5 mmol) and AcOH (0.14 mL, 2.5 mmol) at 78 °C in oil bath and stirred for 21 h. The resulting solution was quenched by saturated Na_2CO_3 aq before separation, the aqueous phase was extracted with AcOEt three times. The organic layers were combined, dried over anhyd Na_2SO_4 and evaporated to afford NH-cyanoenamine **2bi** as a yellow oil which was taken forward without further purification. To a solution of **2bi** and DMAP (3.1 mg, 0.025 mmol) in MeCN (2.0 mL) was added $(Boc)_2O$ (0.23 mL, 1.0 mmol) under nitrogen atmosphere, and then stirred at 50 °C in oil bath for 17 h. The residue was purified by column chromatography with silica gel (*n*-hexane/$CHCl_3$ 5 : 1) to afford **3bi** as a yellow oil (0.099 g, 0.34 mmol, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (s, 9H), 2.36 (t, *J* = 2.5 Hz, 1H), 4.37 (d, *J* = 2.5 Hz, 2H), 5.52 (s, 1H), 7.12 (dd, *J* = 3.8, 5.0 Hz, 1H), 7.51 (dd, *J* = 1.1, 5.0 Hz, 1H), 7.67 (dd, *J* = 1.1, 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.9, 39.7, 73.3, 78.5, 83.1, 89.5, 117.3, 128.2, 129.7, 130.5, 138.3, 152.5; IR (film) cm^{-1}: 1714, 2215; HRMS (ESI+) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{16}N_2NaO_2S$ 311.0830; Found 311.0787.

General procedure for synthesis of pyrrole derivatives

The solution of *N*-Boc enamine in anhydrous THF (2.0 mL) heated at 70 °C in oil bath under N_2 atmosphere. It was added *t*-BuOK (1.5 eq, 1M solution in THF) dropwise and stirred for 5 min. The reaction mixture was quenched by saturated NH_4Cl aq and extracted with AcOEt three times. The organic phase was combined, washed with brine, dried over anhyd Na_2SO_4, evaporated under reduced pressure and purified by column chromatography with silica gel.

1-(2,4-Dimethyl-1*H*-pyrrol-3-yl)ethan-1-one (4aa)[11]

Following the general method, **4aa** was obtained from **3aa** (0.20 mmol) as a white solid (26 mg, 0.19 mmol, 96%) using *n*-hexane/AcOEt 2 : 1 as eluent. Mp 131−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (d, *J* = 1.0 Hz, 3H), 2.43 (s, mo3H), 2.51 (s, 3H), 6.37 (q, *J* = 1.0 Hz, 1H), 7.98 (br, 1H); ^{13}C NMR (100

MHz, $CDCl_3$): δ 13.8, 15.4, 31.1, 114.9, 120.7, 121.1, 135.8, 195.7; IR (KBr) cm^{-1}: 1620, 3230; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_8H_{12}NO$ 138.0919; Found 138.0926.

Cyclohexyl(2,4-dimethyl-1*H*-pyrrol-3-yl)methanone (4ab)

Following the general method, **4ab** was obtained from **3ab** (0.20 mmol) as a white solid (36 mg, 0.18 mmol, 88%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18–1.40 (m, 3H), 1.40–1.54 (m, 2H), 1.66–1.75 (m, 1H), 1.78–1.90 (m, 4H), 2.28 (d, *J* = 1.0 Hz, 3H), 2.49 (s, 3H), 2.91 (tt, *J* = 2.9, 11.4 Hz, 1H), 6.36 (dq, *J* = 1.0, 2.1 Hz, 1H), 8.31 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 15.2, 26.2, 26.3, 29.4, 48.7, 115.0, 120.0, 120.2, 135.7, 202.4; IR (KBr) cm^{-1}: 1614, 3230; HRMS (ESI−) *m/z*: $[M-H]^+$ Calcd for $C_{11}H_{16}NO$ 178.1232; Found 178.1259.

1-(2,4-Dimethyl-1*H*-pyrrol-3-yl)-2,2-dimethylpropan-1-one (4ac)

Following the general method, **4ac** was obtained from **3ac** (0.20 mmol) as a white solid (29 mg, 0.16 mmol, 81%) using *n*-hexane/AcOEt 4 : 1 as eluent. Mp 59−62 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (s, 9H), 2.04 (s, 3H), 2.20 (s, 3H), 6.33–6.38 (m, 1H), 7.78 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.4, 13.5, 27.3, 45.1, 114.5, 117.4, 122.6, 126.4, 213.4; IR (KBr) cm^{-1}: 1705, 3331; HRMS (ESI−) *m/z*: $[M-H]^+$ Calcd for $C_{13}H_{18}NO$ 204.1388; Found 204.1395.

3-Metyl-6,7-dihydro-1*H*-indol-4(5*H*)-one (4ad)[12]

Following the general method, **4ad** was obtained from **3ad** (0.20 mmol) as a brown oil (11 mg, 0.071 mmol, 36%) using *n*-hexane/AcOEt 1 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 (quin, *J* = 6.3 Hz, 2H), 2.30 (d, *J* = 0.9 Hz, 3H), 2.46 (dd, *J* = 5.8, 7.1 Hz, 2H), 2.77 (t, *J* = 6.2 Hz, 2H), 6.40 (d, *J* = 0.9 Hz, 1H), 8.08 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8, 23.3, 24.2, 38.8, 116.0, 118.9, 119.3, 143.7, 195.8; IR (KBr) cm^{-1}: 1630, 3213; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_9H_{12}NO$ 150.0919; Found 150.0926.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(phenyl)methanone (4ae)

Following the general method, **4ae** was obtained from **3ae** (0.20 mmol) as a yellow solid (32 mg, 0.16 mmol, 81%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 126−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.00 (d, *J* = 1.0 Hz, 3H), 2.13 (s, 3H), 6.38 (q, *J* = 1.0 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.69 (d, *J* = 7.3 Hz, 2H), 8.62 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.3, 13.9, 115.3, 120.7, 120.8, 128.3, 129.0, 131.5, 135.0, 141.5, 194.9; IR (KBr) cm^{-1}: 1572, 1613, 3222; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{14}NO$ 200.1075; Found 200.1077.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(*p*-tolyl)methanone (4af)

Following the general method, **4af** was obtained from **3af** (0.20 mmol) as a yellow solid (38 mg, 0.18 mmol, 90%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 108−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.00 (d, *J* = 1.0 Hz, 3H), 2.13 (s, 3H), 2.40 (s, 3H), 6.37 (s, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 8.74 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.3, 13.8, 21.7, 115.3, 120.6, 120.8, 129.0, 129.3, 134.6, 138.6, 142.1, 194.8; IR (KBr) cm^{-1}: 1604, 3238; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{14}H_{14}NO$ 212.1075; Found 212.1058.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(4-methoxyphenyl)methanone (4ag)

Following the general method, **4ag** was obtained from **3ag** (0.20 mmol) as a yellow oil (38 mg, 0.17 mmol, 83%) using *n*-hexane/AcOEt 3 : 2 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.01 (d, *J* = 1.0 Hz, 3H), 2.21 (s, 3H), 3.87 (s, 3H), 6.43 (q, *J* = 1.0 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.8 Hz, 2H), 7.92 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.1, 13.6, 55.5, 113.5, 115.2, 120.4, 120.9, 131.6, 133.8, 133.9, 162.6, 193.8; IR (KBr) cm^{-1}: 1600, 3347; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{14}H_{14}NO_2$ 228.1025; Found 228.1010.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(4-fluorophenyl)methanone (4ah)

Following the general method, **4ah** was obtained from **3ah** (0.22 mmol) as a yellow oil (41 mg, 0.19 mmol, 86%) using *n*-hexane/AcOEt 2 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.99 (d, *J* = 1.0 Hz, 3H), 2.21 (s, 3H), 6.43 (q, *J* = 1.0 Hz, 1H), 7.11 (t, *J* = 8.7 Hz, 2H), 7.74 (dd, *J* = 5.5, 8.7 Hz, 2H), 7.96 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.3, 13.8, 115.4 (d, *J* = 21.6 Hz), 115.5, 120.5, 120.6, 131.6 (d, *J* = 9.0 Hz), 134.7, 137.6 (d, *J* = 3.0 Hz), 165.0 (d, *J* = 252.2 Hz), 193.4; IR (KBr) cm^{-1}: 1603, 3221; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{13}H_{11}FNO$ 216.0825; Found 216.0817.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(4-chlorophenyl)methanone (4ai)

Following the general method, **4ai** was obtained from **3ai** (0.20 mmol) as a yellow oil (37 mg, 0.16 mmol, 79%) using *n*-hexane/AcOEt 2 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.98 (d, *J* = 1.0 Hz, 3H), 2.19 (s, 3H), 6.41 (q, *J* = 1.0 Hz, 1H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 8.23 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.3, 13.9, 115.6, 120.4, 120.7, 128.6, 130.5, 135.1, 137.7, 139.7, 193.5; IR (KBr) cm^{-1}: 1604, 3228; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{13}H_{11}ClNO$ 232.0529; Found 232.0523.

4-(2,4-Dimethyl-1*H*-pyrrole-3-carbonyl)benzonitrile (4aj)

Following the general method, **4aj** was obtained from **3aj** (0.20 mmol) as a yellow solid (37 mg, 0.16 mmol, 82%) using *n*-hexane/AcOEt 1 : 1 as eluent. Mp 157−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.94 (d, *J* = 1.1 Hz, 3H), 2.21 (s, 3H), 6.44 (dq, *J* = 1.1, 2.2 Hz, 1H), 7.71–7.79 (m, 4H), 8.05 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.5, 14.1, 114.4, 115.9, 118.4, 119.8, 120.7, 129.1, 132.3, 136.2, 145.5, 192.7; IR (KBr) cm^{-1}: 1617, 2230, 3300; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{14}H_{11}N_2O$ 223.0871; Found 223.0874.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(*m*-tolyl)methanone (4ak)

Following the general method, **4ak** was obtained from **3ak** (0.20 mmol) as a yellow oil (39 mg, 0.18 mmol, 92%) using *n*-hexane/AcOEt 2 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.00 (d, *J* = 1.0 Hz, 3H), 2.19 (s, 3H), 2.40 (s, 3H), 6.42 (q, *J* = 1.0 Hz, 1H), 7.29−7.33 (m, 2H), 7.46−7.54 (m, 2H), 8.00 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.3, 13.9, 21.4, 115.3, 120.7, 120.8, 126.3, 128.2, 129.5, 132.2, 134.9, 138.0, 141.4, 195.1; IR (KBr) cm^{-1}: 1609, 3196; HRMS (ESI−) *m/z*: [M−H]$^+$ $C_{14}H_{14}NO$ 212.1075; Found 212.1073.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(*o*-tolyl)methanone (4al)

Following the general method, **4al** was obtained from **3al** (0.20 mmol) as a yellow solid (28 mg, 0.13 mmol, 66%) using *n*-hexane/AcOEt 2 : 1 as eluent. Mp 159−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.94 (d, *J* = 1.0 Hz, 3H), 2.09 (s, 3H), 2.32 (s, 3H), 6.36 (q, *J* = 1.0 Hz, 1H), 7.18−7.33 (m, 4H), 8.10 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.4, 13.9, 19.4, 115.5, 120.7, 121.4, 125.8, 127.0, 129.2, 130.7, 134.7, 137.2, 142.9, 196.1; IR (KBr) cm^{-1}: 1598, 3208; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{14}H_{14}NO$ 212.1075; Found 212.1070.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(thiophen-2-yl)methanone (4am)

Following the general method, **4am** was obtained from **3am** (0.20 mmol) as a orange oil (36 mg, 0.18 mmol, 88%) using *n*-hexane/AcOEt 3 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (d, *J* = 1.0 Hz, 3H), 2.29 (s, 3H), 6.44 (dq, *J* = 1.0, 2.0 Hz, 1H), 7.10 (dd, *J* = 3.7, 4.9 Hz, 1H), 7.51 (dd, *J* = 1.1, 3.7 Hz, 1H), 7.61 (dd, *J* = 1.1, 4.9 Hz, 1H), 7.95 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.9, 13.6, 115.5, 119.9, 121.0, 127.6, 132.7, 133.2, 133.6, 146.3, 186.4; IR (film) cm^{-1}: 1595, 3291; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{11}H_{10}NOS$ 204.0483; Found 204.0488.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(furan-2-yl)methanone (4an)

Following the general method, **4an** was obtained from **3an** (0.20 mmol) as a yellow solid (32 mg, 0.17 mmol, 84%) using *n*-hexane/AcOEt 2 : 1 as eluent. Mp 113−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.11 (d, *J* = 1.0 Hz, 3H), 2.31 (s, 3H), 6.44 (dq, *J* = 1.0, 2.1 Hz, 1H), 6.54 (dd, *J* = 1.7, 3.5 Hz, 1H), 7.09 (dd, *J* = 0.6, 3.5 Hz, 1H), 7.59 (dd, *J* = 0.6, 1.7 Hz, 1H), 7.97 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7, 13.5, 112.1, 115.3, 117.9, 120.3, 120.4, 133.6, 145.7, 154.2, 181.2; IR (KBr) cm^{-1}: 1595, 3204; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{11}H_{10}NO_2$ (M−H$^+$) 188.0712; Found 188.0722.

(2,4-Dimethyl-1*H*-pyrrol-3-yl)(pyridin-3-yl)methanone (4ao)

Following the general method, **4ao** was obtained from **3ao** (0.20 mmol) as a yellow solid (28 mg, 0.14 mmol, 69%) using *n*-hexane/AcOEt 1 : 3 as eluent. Mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.99 (d, *J* = 1.0 Hz, 3H), 2.23 (s, 3H), 6.45 (dq, *J* = 1.0, 2.1 Hz, 1H), 7.40 (ddd, *J* = 0.8, 4.9, 7.8 Hz, 1H), 8.00 (dt, *J* = 2.0, 7.8 Hz, 1H), 8.25 (br, 1H), 8.73 (dd, *J* = 2.0, 4.9 Hz, 1H), 8.87 (dd, *J* = 0.8, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.6, 14.2, 115.7, 120.4, 120.8, 123.5, 135.6, 136.3, 137.0, 150.2, 151.9, 192.1; IR (KBr) cm^{-1}: 1590, 1624, 3175; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{12}H_{11}N_2O$ 199.0871; Found 199.0872.

1-(4-Benzyl-2-methyl-1*H*-pyrrol-3-yl)ethan-1-one (4ap)

Following the general method, **4ap** was obtained from **3ap** (0.20 mmol) as a yellow solid (35 mg, 0.16 mmol, 82%) using *n*-hexane/AcOEt 2 : 1 as eluent. Mp 158−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37

(s, 3H), 2.51 (s, 3H), 4.07 (s, 2H), 6.10−6.14 (m, 1H), 7.15−7.30 (m, 5H), 8.27 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.5, 31.0, 33.9, 116.0, 120.5, 125.1, 125.9, 128.4, 128.9, 135.9, 141.3, 195.5; IR (KBr) cm^{-1}: 1617, 3205; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{16}NO$ 214.1232; Found 214.1249.

1-(4-(4-Chlorobenzyl)-2-methyl-1*H*-pyrrol-3-yl)ethan-1-one (4aq)

Following the general method, **4aq** was obtained from **3aq** (0.20 mmol) as a yellow solid (39 mg, 0.16 mmol, 79%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 169−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H), 2.52 (s, 3H), 4.03 (s, 2H), 6.14−6.16 (m, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 8.14 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.7, 31.0, 33.2, 115.9, 120.5, 124.9, 128.4, 130.3, 131.6, 135.7, 140.0, 195.2; IR (KBr) cm^{-1}: 1620, 3207; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{15}ClNO$ 248.0842; Found 248.0857.

1-(4-((4-Acetyl-5-methyl-1*H*-pyrrol-3-yl)methyl)phenyl)ethan-1-one (4ar)

Following the general method, **4ar** was obtained from **3ar** (0.20 mmol) as a yellow solid (7.8 mg, 0.031 mmol, 15%) using *n*-hexane/AcOEt 1 : 1 as eluent. Mp 159−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H), 2.54 (s, 3H), 2.58 (s, 3H), 4.13 (s, 2H), 6.19−6.21 (m, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.98 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.6, 26.6, 30.9, 33.7, 115.8, 120.5, 124.2, 128.4, 129.0, 135.0, 135.4, 147.5, 194.8, 198.1; IR (KBr) cm^{-1}: 1616, 1678, 3205; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{18}NO_2$ 256.1338; Found 256.1350.

1-(4-(4-Methoxybenzyl)-2-methyl-1*H*-pyrrol-3-yl)ethan-1-one (4as)

Following the general method, **4as** was obtained from **3as** (0.20 mmol) as a yellow solid (27 mg, 0.11 mmol, 55%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 2.52 (s, 3H), 3.79 (s, 3H), 4.00 (s, 2H), 6.11−6.14 (m, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 8.7 Hz, 2H), 7.93 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.5, 31.0, 33.0, 55.3, 113.7, 115.9, 120.4, 125.6, 129.8, 133.4, 136.0, 157.8, 195.6; IR (KBr) cm^{-1}: 1620, 3207; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{18}NO_2$ 244.1338; Found 244.1355.

Ethyl 4-(4-chlorobenzyl)-2-methyl-1*H*-pyrrole-3-carboxylate (4at)[13]

Following the general method, **4at** was obtained from **3at** (0.20 mmol) as a yellow solid (37 mg, 0.13 mmol, 67%) using *n*-hexane/AcOEt 6 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, *J* = 7.1 Hz, 3H), 2.51 (s, 3H), 4.01 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 6.16−6.18 (m, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.94 (br, 1H).

(4-(4-Chlorobenzyl)-2-methyl-1*H*-pyrrol-3-yl)(phenyl)methanone (4au)

Following the general method, **4au** was obtained from **3au** (0.20 mmol) as a yellow solid (33 mg, 0.11 mmol, 54%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 137−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 3H), 3.81 (s, 2H), 6.28−6.31 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.64 (d, *J* = 7.4 Hz, 2H), 7.97 (br, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 14.0, 32.3, 116.1, 120.0, 124.9, 128.3, 128.4, 128.9, 130.2, 131.4, 131.7, 135.0, 140.2, 141.3, 194.7; IR (KBr) cm^{-1}: 1594, 3270; HRMS (ESI+) *m/z*: [M+H]$^+$ Calcd for $C_{19}H_{17}ClNO$ 310.0999; Found 310.1004.

Ethyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (4av)[14]

Following the general method, **4av** was obtained from **3av** (0.20 mmol) as a yellow oil (36 mg, 0.18 mmol, 89%) using *n*-hexane/AcOEt 4 : 1 as eluent. ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.35 (t, *J* = 7.1 Hz, 3H), 2.24 (d, *J* = 1.0 Hz, 3H), 2.49 (s, 3H), 4.27 (q, *J* = 7.1 Hz, 2H), 6.36 (q, *J* = 1.0 Hz, 1H), 7.96 (br, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 12.8, 14.2, 14.6, 59.2, 110.9, 114.3, 121.7, 136.0, 166.5; IR (KBr) cm^{-1}: 1667, 3309; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_9H_{12}NO_2$ 166.0868; Found 166.0870.

***iso*-Propyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (4aw)**

Following the general method, **4aw** was obtained from **3aw** (0.20 mmol) as a yellow oil (29 mg, 0.16 mmol, 81%) using *n*-hexane/AcOEt 5 : 1 as eluent. ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.32 (d, *J* = 6.2 Hz, 6H), 2.24 (d, *J* = 1.1 Hz, 3H), 2.49 (s, 3H), 5.18 (sept, *J* = 6.2 Hz, 1H), 6.35 (q, *J* = 1.1 Hz, 1H), 7.86 (br, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 12.8, 14.2, 22.4, 66.3, 111.2, 114.3, 121.7, 135.9, 166.0; IR (film) cm^{-1}: 1667, 3318; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{10}H_{14}NO_2$ 180.1025; Found 180.1025.

***tert*-Butyl 2,4-dimethyl-1*H*-pyrrole-3-carboxylate (4ax)**

Following the general method, **4ax** was obtained from **3ax** (0.20 mmol) as a white solid (36 mg, 0.18 mmol, 92%) using *n*-hexane/AcOEt 6 : 1 as eluent. Mp 137−140 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.56 (s, 9H), 2.20 (d, *J* = 1.1 Hz, 3H), 2.47 (s, 3H), 6.34 (q, *J* = 1.1 Hz, 1H), 7.82 (br, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 12.9, 14.3, 28.8, 79.3, 112.3, 114.1, 121.6, 135.4, 165.8; IR (KBr) cm^{-1}: 1665, 3303; HRMS (ESI−) *m/z*: [M−H]$^+$ Calcd for $C_{11}H_{16}NO_2$ 194.1181; Found 194.1164.

4-Methyl-2-phenyl-1*H*-pyrrole-3-carbonitrile (4ay)[4b]

Following the general method, **4ay** was obtained from **3ay** (0.10 mmol) as a white solid (15 mg, 0.083 mmol, 83%) using *n*-hexane/AcOEt 1 : 1 as eluent. ^{1}H NMR (400 MHz, CDCl$_3$): δ 2.22 (s, 3H), 6.60 (s, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.67 (d, *J* = 7.4, 2H), 8.78 (s, 1H).

4-Methyl-2-(*p*-tolyl)-1*H*-pyrrole-3-carbonitrile (4az)[4b]

Following the general method, **4az** was obtained from **3az** (0.10 mmol) as a brown solid (14 mg, 0.072 mmol, 72%) using *n*-hexane/AcOEt 2 : 1 as eluent. ^{1}H NMR (400 MHz, CDCl$_3$): δ 2.22 (d, *J* = 1.0 Hz, 3H), 2.38 (s, 3H), 6.57 (q, *J* = 1.0 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 2H), 8.57 (br, 1H).

2-(4-Methoxyphenyl)-4-methyl-1*H*-pyrrole-3-carbonitrile (4ba)[4b]

Following the general method, **4ba** was obtained from **3ba** (0.10 mmol) as a brown solid (15 mg, 0.075 mmol, 73%) using *n*-hexane/AcOEt 1 : 1 as eluent. ^{1}H NMR (400 MHz, CDCl$_3$): δ 2.21 (d, *J* = 1.0 Hz, 3H), 3.83 (s, 3H), 6.55 (q, J = 1.0 Hz, 1H), 6.95 (d, J = 8.9 Hz, 2H), 7.60 (d, J = 8.9 Hz, 2H), 8.54 (br, 1H).

2-(4-Fluorophenyl)-4-methyl-1*H*-pyrrole-3-carbonitrile (4bb)[4b]

Following the general method, **4bb** was obtained from **3bb** (0.10 mmol) as a brown solid (17 mg, 0.087 mmol, 84%) using *n*-hexane/AcOEt 2 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (d, J = 1.1 Hz, 3H), 6.60 (q, J = 1.1 Hz, 1H), 7.12 (t, J = 8.8 Hz, 2H), 7.64 (dd, J = 5.1, 8.8 Hz, 2H), 8.75 (br, 1H).

2-(4-Chlorophenyl)-4-methyl-1*H*-pyrrole-3-carbonitrile (4bc)[4b]

Following the general method, **4bc** was obtained from **3bc** (0.10 mmol) as a white solid (18 mg, 0.084 mmol, 83%) using *n*-hexane/AcOEt 1 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.23 (s, 3H), 6.63 (s, 1H), 7.43 (d, J = 8.7 Hz, 2H), 7.61 (d, J = 8.7 Hz, 2H), 8.44 (s, 1H).

2-(4-Bromophenyl)-4-methyl-1*H*-pyrrole-3-carbonitrile (4bd)[4b]

Following the general method, **4bd** was obtained from **3bd** (0.92 mmol) as a brown solid (20 mg, 0.077 mmol, 84%) using *n*-hexane/AcOEt 3 : 1 as eluent. ^{1}H NMR (400 MHz, CD_3OD): δ 2.19 (d, J = 1.0 Hz, 3H), 6.70 (q, J = 1.0 Hz, 1H), 7.61 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 9.0 Hz, 2H).

2-(4-Cyanophenyl)-4-methyl-1*H*-pyrrole-3-carbonitrile (4be)

Following the general method, **4be** was obtained from **3be** (0.10 mmol) as a yellow solid (13 mg, 0.062 mmol, 61%) using *n*-hexane/AcOEt 1 : 1 as eluent. Mp 207−209 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25 (d, J = 0.9 Hz, 3H), 6.72 (q, J = 0.9 Hz, 1H), 7.74 (d, J = 8.7 Hz, 2H), 7.80 (d, J = 8.7 Hz, 2H), 8.66 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.6, 93.3, 112.0, 118.0, 119.5, 120.6, 125.7, 126.8, 134.0, 136.0, 136.8; IR (KBr) cm^{-1}: 2224, 2440, 3267; HRMS (ESI−) *m/z*: $[M-H]^+$ Calcd for $C_{13}H_8N_3$ 206.0718; Found 206.0705.

4-Methyl-2-(*m*-tolyl)-1*H*-pyrrole-3-carbonitrile (4bf)

Following the general method, **4bf** was obtained from **3bf** (0.10 mmol) as a brown solid (15 mg, 0.076 mmol, 75%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 168−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.22 (d, J = 1.1 Hz, 3H), 2.39 (s, 3H), 6.57 (q, J = 1.1 Hz, 1H), 7.17 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 7.8 Hz, 1H), 7.45−7.50 (m, 2H), 8.55 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.8, 21.6, 91.6, 116.7, 117.5, 122.8, 124.3, 126.2, 129.3, 129.5, 130.1, 138.8, 139.1; IR (KBr) cm^{-1}: 2215, 3283; HRMS (ESI−) *m/z*: $[M-H]^+$ Calcd for $C_{13}H_{11}N_2$ 195.0922; Found 195.0916.

4-Methyl-2-(*o*-tolyl)-1*H*-pyrrole-3-carbonitrile (4bg)

Following the general method, **4bg** was obtained from **3bg** (0.10 mmol) as a brown solid (14 mg, 0.072 mmol, 69%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 119−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.22 (d, J = 0.7 Hz, 3H), 2.36 (s, 3H), 6.58 (q, J = 1.0 Hz, 1H), 7.20−7.38 (m, 4H), 8.37 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.8, 20.3, 94.1, 116.3, 117.1, 123.1, 126.2, 129.3, 130.0, 130.0, 131.0, 136.7, 139.2; IR (KBr) cm^{-1}: 2219, 3284; HRMS (ESI−) *m/z*: $[M-H]^+$ Calcd for $C_{13}H_{11}N_2$ 195.0922; Found 195.0916.

2-(Furan-2-yl)-4-methyl-1*H*-pyrrole-3-carbonitrile (4bh)[4b]

Following the general method, **4bh** was obtained from **3bh** (0.10 mmol) as a brown solid (17 mg, 0.096 mmol, 92%) using *n*-hexane/AcOEt 3 : 1 as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.20 (d, *J* = 1.1 Hz, 3H), 6.51 (dd, *J* = 1.8, 3.5 Hz, 1H), 6.55 (q, *J* = 1.1 Hz, 1H), 6.91 (dd, *J* = 0.6, 3.5 Hz, 1H), 7.41 (dd, *J* = 0.6, 1.8 Hz, 1H), 8.72 (br, 1H).

4-Methyl-2-(thiophen-2-yl)-1*H*-pyrrole-3-carbonitrile (4bi)

Following the general method, **4bi** was obtained from **3bi** (0.10 mmol) as a red solid (13 mg, 0.071 mmol, 69%) using *n*-hexane/AcOEt 3 : 1 as eluent. Mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (d, *J* = 1.0 Hz, 3H), 6.55 (q, *J* = 1.0 Hz, 1H), 7.09 (dd, *J* = 3.7, 5.1 Hz, 1H), 7.30 (dd, *J* = 1.1, 5.1 Hz, 1H), 7.46 (dd, *J* = 1.1, 3.7 Hz, 1H), 8.56 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.8, 91.9, 116.6, 116.9, 124.1, 124.9, 125.3, 128.3, 132.1, 133.3; IR (KBr) cm^{-1}: 2217, 3260; HRMS (ESI+) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_9N_2S$ 189.0486; Found 189.0443.

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